“CLINICAL AND BACTERIOLOGICAL PROFILE IN LYMPH NODE AND BONE TUBERCULOSIS”

Dissertation submitted to The Tamil Nadu Dr.M.G.R. Medical University in partial fulfilment of the requirements for

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THE TAMIL NADU DR. M.G.R. MEDICAL UNIVERSITY

CHENNAI, INDIA.

APRIL, 2016.

BONAFIDE CERTIFICATE

This is to certify that the dissertation titled "**CLINICAL AND BACTERIOLOGICAL PROFILE IN LYMPH NODE AND BONE TUBERCULOSIS**" is a bonafide work done by **Dr. N.Muthulakshmi,** Post Graduate student of the Institute of Thoracic Medicine, Rajiv Gandhi Government General Hospital, Madras Medical College, Chennai-3, during the academic year 2012-2014,2015-2016. This work has not previously formed the basis for the award of any degree.

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This is to certify that the dissertation titled "**CLINICAL AND BACTERIOLOGICAL PROFILE IN LYMPH NODE AND BONE TUBERCULOSIS**" is a bonafide work done by **Dr. N. Muthulakshmi** during her **MD (Tuberculosis and Respiratory Diseases)** course in the academic years 2012-2014, 2015-2016 at the Institute of Thoracic Medicine and Rajiv Gandhi Government General Hospital – Madras Medical College, Chennai under my guidance.

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I, **Dr. N.Muthulakshmi**, solemnly declare that this dissertation titled **"CLINICAL AND BACTERIOLOGICAL PROFILE IN LYMPH NODE AND BONE TUBERCULOSIS"** is a bonafide work done by me at Madras Medical College during 2012-2014,2015-2016 under the guidance and supervision of **Prof. Dr.D.Ranganathan MD,DTCD,DNB.,** Professor and Director, Institute of Thoracic Medicine, Madras Medical College, Chennai-600003.

This dissertation is submitted to The Tamil Nadu Dr.M.G.R.Medical University, Chennai towards partial fulfillment of the rules and regulations for the award of **M.D Degree in Tuberculosis and Respiratory Diseases(Branch-XVII).**

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CONTENTS

Title: Clinical and bacteriological profile in lymph node and bone tuberculosis.

Aims and objectives:

1. To study the clinical data and histopathological and microbiological correlates in clinical suspects of lymph node and bone tuberculosis.

2. To study the pattern of drug resistance in microbiologically confirmed cases of lymph node and bone tuberculosis.

Materials and Methods:

114 patients with clinical suspicion of spine(31) and lymph node tuberculosis(83) in whom treating doctor(pulmonologist, general surgeon, orthopaedician) has suggested surgical intervention for diagnostic/therapeutic reasons were enrolled in the study after obtaining informed consent. The clinical history regarding present complaints, past history of anti-tuberculous treatment (ATT) and co-morbidities were taken. Investigations including complete hemogram, antibody test for HIV, Random Blood Sugar, Chest X ray were done for all patients. Other investigations were done as clinically indicated. Preoperative evaluation was done and patients were posted for surgery after obtaining fitness from anaesthetist. Surgical specimens including excision biopsy specimens, pus, bone debris were obtained and were sent for histopathological examination to pathology lab and for AFB smear examination by Ziehl Neelson method, AFB solid culture in LJ medium and drug susceptibility testing(DST) by 1% proportion method to National Reference Laboratory, National Institute for Research in Tuberculosis, Chetpet, Chennai.

Results

We defined a case of lymph node and bone tuberculosis if granulomas were present in histopathology or if LJ culture showed growth and identified as Mycobacterium tuberculosis or both. The case definition based on histology and microbiology was met by 86.8%(99/114) of clinical suspects of lymph node and bone tuberculosis. Most of the patients of lymph node tuberculosis were in the age group of 11-20 years and of bone tuberculosis were in the age group of 31-40 years. Lymph node tuberculosis was more common in females with a male to female ratio of 3:5 and bone tuberculosis more common in males with a male to female ratio of 2:1. There was histopathological evidence of granulomas in 80%(91/114) of clinical suspects of lymph node and bone tuberculosis. Mycobacterium tuberculosis was isolated from 26.2% (26/99)of clinical suspects of lymph node and bone tuberculosis. Of the culture isolates 23% showed non granulomas in histology, of these 60% were HIV seropositive and 40% diabetic. It is inferred that immune suppression interferes with eliciting a granulomatous response and hence in patients with immune suppression tuberculosis should be considered even in the absence of granulomas in histology. The multi drug resistant rate is 22% in previously treated patients compared to none of the new patients. The resistance rate in HIV patients is 37.5% and in HIV negative patients is 27.7%.

Conclusion

In our study we observed the culture yield to be low due to paucibacillary nature of the disease in concordance with earlier studies. In immune compromised state like HIV and diabetes nongranulomatous histology in lymph node and spine TB were noted. Lymph node and bone tuberculosis have a higher degree of drug resistance in previously treated patients and HIV seropositive patients. These groups can be considered as risk factors for drug

resistance in lymph node and bone tuberculosis and can be targeted for drug susceptibility testing(DST).

Key words:- extra pulmonary tuberculosis, tuberculous lymphadenitis, Pott's spine, drug resistant tuberculosis, multi drug resistant tuberculosis, LJ culture.

INTRODUCTION

Scourge, phthisis, phyma, hectic fever, consumption, white death, white plague, struma, the names are plenty and also notoriously described by John Bunyan as 'captain of all men of death' is the disease tuberculosis known to man since time immemorial. The fight against tuberculosis has been fought for ages. The disease has taken its toll on humans since long and continues to do so.

Tuberculosis is an ancient infection that has plagued humans throughout history. It has been referred to in the Vedas as 'rajayakshma'. There is clear evidence to show that the infection existed dating back to 8000 B.C., from skeletal remains of prehistoric humans in Germany.[1,2]

Tuberculosis is one of the leading causes of mortality in India killing 2 persons every three minutes, nearly 1000 every day.[3]

The clinical manifestations of tuberculosis are of two types: Pulmonary and Extra-pulmonary forms of tuberculosis(EPTB), pulmonary being the commonest.

Extra pulmonary tuberculosis is defined as tuberculosis of organs other than the lungs, such as pleura, lymph nodes, abdomen, genito-urinary tract, skin, joints, bones, tubercular meningitis, tuberculoma of the brain, etc.[4] Diagnosis is based on atleast one specimen with confirmed Mycobacterium tuberculosis from the extrapulmonary site; or histological evidence; or strong clinical evidence

consistent with active extra pulmonary tuberculosis disease followed by a medical officer's decision to treat with a full course of anti-tuberculous therapy.[4,5]

As tuberculosis infection is spread by aerosol, pulmonary tuberculosis is the most common form of the disease. Extra pulmonary tuberculosis is usually a consequence or accompaniment of pulmonary tuberculosis.

The problem of drug resistant tuberculosis has been recognised since the advent of the first anti tuberculous drug. The problem of drug resistance is now a major hindrance in our war against this centuries old disease. According to global TB report 2014, 3.5% of new patients and 20.5% of previously treated patients have multidrug resistant tuberculosis (MDR-TB). In 2013, an estimated 4,80,000 new cases of MDR-TB were reported globally, and approximately 2,10,000 deaths were reported due to multidrug resistant tuberculosis (MDR-TB). More than half of MDR TB patients were in India, China and the Russian Federation. Extremely drug resistant tuberculosis (XDR-TB) is reported in 9% of patients with multidrug resistant tuberculosis (MDR-TB).[6]

The main focus of international and national control strategies is on pulmonary tuberculosis it being the transmissible form of disease. However extra pulmonary tuberculosis including lymph node and bone tuberculosis adds significantly to the burden of disease and requires early, accurate diagnosis. Prompt diagnosis is hindered by the difficulty in obtaining adequate,

representative samples, high rates of contamination, lack of gold standard diagnostic tests and the low yield of conventional cultures. There is a need for large multi centric epidemiologic trials to study the risk factors and patterns of drug resistance in extra pulmonary tuberculosis and direction of resources towards high risk individuals for drug susceptibility testing.

Much of the reported data worldwide is on pulmonary tuberculosis, hence we undertook this study to analyse the clinical and bacteriological charecteristics in extrapulmonary tuberculosis confining ourserlves to lymph node and bone tuberculosis in particular spine tuberculosis.

REVIEW OF LITERATURE

Extra pulmonary tuberculosis constitutes 15-20% of total cases of tuberculosis in immune hosts and 50% of total cases of tuberculosis in immune compromised hosts.[7] The most common site of involvement of extra pulmonary tuberculosis is lymph node, followed by pleural effusion.[8]

The clinical presentation of extra pulmonary tuberculosis is atypical and includes a wide array of differential diagnosis. It is difficult to obtain samples for diagnosis and the yields are poor by conventional methods. For managing complications and for diagnosis, surgical means may be required to procure tissue samples.[8]

Pulmonary tuberculosis being the main transmissible form of tuberculosis has received the main focus in international control strategies. Extra pulmonary tuberculosis also significantly contributes to the burden of disease and hence requires special attention.[9]

On analysing the reasons for incorrect estimation of extra pulmonary tuberculosis, difference in terminology was found to be an important reason. Some authors included pleural tuberculosis as a form of extra pulmonary tuberculosis while others considered lungs and the covering pleura to be a single organ and ascribed both organs to pulmonary tuberculosis.[9]

In a descriptive analysis done in European Union(EU)/ European Economic Area(EEA) to study the burden and trends of extra pulmonary

tuberculosis by Sandgren et al., in 2013 notification rates of tuberculosis from 2002 to 2011 decreased due to decrease in pulmonary tuberculosis but for extra pulmonary tuberculosis the notification rates remained stable[3.4/100000 in 2002 and 3.2/100000 in 2011]. Hence they inferred that proportion of extra pulmonary tuberculosis showed a rising trend from 2002(16.4%) to 2011(22.4%). In their study 33.7% cases of extra pulmonary tuberculosis were culture confirmed. They concluded that while pulmonary tuberculosis showed a falling trend, extra pulmonary tuberculosis showed a rising trend.[10]

A negative smear for acid fast bacillus, negative culture and absence of granulomas does not rule out the diagnosis of extra pulmonary tuberculosis.[11] Golden MP et al., suggested high clinical index of suspicion in absence of diagnostic proof and absence of alternate diagnosis favours the diagnosis of tuberculosis.

Excisional biopsy of lymph nodes with its histopathology, smear for Acid Fast Bacillus and Lowenstein-Jensen culture are the diagnostic tests of choice for lymph node tuberculosis. Fine needle aspiration is more reliable in HIV seroreactive patients because of high bacillary load.[12]

Hematological manifestations are common in extrapulmonary disease due to systemic involvement by dissemination. Anemia, increased or decreased leucocyte counts, increased or decreased platelets, monocytosis and rarely pancytopenia are associated with extrapulmonary tuberculosis.[13]

Positive findings in chest x ray or positive tuberculin skin test supports the diagnosis but negative results do not rule out extrapulmonary tuberculosis.[14] Shadows suggestive of healed tuberculous lesion are present in chest roentgenograms of approximately 50% of patients with osteoarticular tuberculosis but active pulmonary tuberculosis is rare.[15]

The diagnosis of peritoneal, urogenital and meningeal tuberculosis is more difficult due to wide options of differential diagnosis and low sensitivity of diagnostic tests both conventional and Polymerase Chain Reaction(PCR) based tests.[8]

The radiological differential diagnosis of most forms of extrapulmonary tuberculosis includes metastatic disease and low grade pyogenic infections like brucellosis, fungal infections and sarcoidosis.[14] Lymph nodes showing peripheral rim enhancement and low attenuation centres are more commonly seen in tuberculosis but are also seen in lymphoma, inflammatory conditions and metastatic malignancies.[16]

Drug Resistant Tuberculosis:

Drug resistance is defined as temporary or permanent capacity of organisms and their progeny to stay viable or multiply in presence of drug concentrations that would destroy or inhibit growth normally.

Types of drug resistance:

1. Primary:

   Drug resistance in patients without previous history of treatment for tuberculosis, possibly their source of infection being drug resistant cases.

2. Acquired:

   Patients who were infected with drug sensitive bacilli, but later developed resistance to one or more of the drugs. Acquired drug resistance is usually due to inappropriate regimens, inadequate dosages and non adherence by patients.[17]

The thought of antibiotic resistance against drugs was first recognised shortly after the discovery of streptomycin in 1944, when they observed that a substantial proportion of patients treated with streptomycin had a relapse following an apparent cure. The phenomenon of fall of susceptible organisms followed by a rise of resistant organisms was appreciated leading to the recommendations for multi drug therapy.

Abdulrahman A Alrajhi et al, observed that young age and history of past treatment with tuberculosis drugs were risk factors among patients with drug resistant tuberculosis.[18]

Gneya Bhatt et al., observed that prior history of lost to follow up and poor socioeconomic conditions were risk factors for drug resistant tuberculosis.[19]

Girma Mulisa et al., reported history of contact with a case of tuberculosis, alcohol abuse, farming by occupation, retroviral disease and previous treatment as risk factors for drug resistant tuberculosis.[20]

Lymph Node Tuberculosis:

Lymph node tuberculosis, the most common form of extra pulmonary tuberculosis was known as the King's evil during the Middle Ages. It was believed that royal touch cured scrofula and the gift of gold coin from the king prevented further scrofulous attacks.[21] Historically lymph node TB is more common in children.

Multiplicity, matting and caseation are the three clinching points favouring the diagnosis of tuberculous lymphadenitis. If the offending node is below the deep fascia through which it may break through it results in a subcutaneous caseous collection (collar-stud abscess). As the disease process reaches the surface, skin gets involved producing scrofuloderma or tuberculous dermatitis.

Lymph node tuberculosis may be a part of primary or post primary disease. In children with lymph node TB 50-80% have radiographic evidence of active pulmonary tuberculosis which is in concordance with Walgren's

calendar for primary tuberculosis published in 1948. In striking contrast in adults with tuberculous lymphadenitis only 30% show chest x ray abnormality and the abnormality is usually of old healed tuberculous lesion and the lymph node disease is part of post primary or reactivation disease. Walgren's calendar[22] depicting the sequence of events in primary tuberculosis is presented below.

Stage	Duration	Features
1	3-8 weeks	The primary complex develops. Conversion to tuberculin positivity occurs.
2	About 3 months	Life threatening forms of disease due to hematogenous dissemination occur i.e. tuberculous meningitis and military tuberculosis.
3	3-4 months	Tuberculous pleurisy may be the result of either hematogenous spread or direct spread from an enlarging primary focus.
4	Up to 3 years	This stage lasts until the primary complex resolves. More slowly developing extra pulmonary lesions, particularly in the bones and joints, may appear.
5	Up to 12 years	Genitourinary tuberculosis may occur as a late manifestation of primary tuberculosis.

In the West historically lymph node TB was caused mainly by mycobacterium bovis but in India the cirucumstances are different. The habit of consuming boiled milk and cows being relatively immune to the tuberculosis of the udder, Mycobacterium tuberculosis causes nearly all cases of tuberculous lymphadenitis.

Mediastinal nodes inspite of being the primary draining sites, account for less than 5% cases of reported lymph node TB. Clinically apparent tuberculous lymphadenitis commonly involves nodes of head and neck. Infection in these nodes commonly results from generalised lymphatic spread from a primary lung infection, since localised primary infections are unusual in head and neck.

The possible events in lymph node TB are compression of surrounding tissue, caseation, breakdown and healing of eroded nodes causing fibrotic remnants. Even though mortality is uncommon, morbidity and chronic illness is common.

In general tuberculous lymphadenitis is most common in cervical region, but inguinal, axillary, mediastinal, mesenteric and intramammary involvement also occurs.[23]

The common sites of tuberculous lympadenitis in head and neck region are

1. Anterior and posterior cervical
2. Submandibular
3. Preauricular
4. Submental [24]

The differential diagnosis includes chronic septic lymphadenitis, Hodgkin's disease, secondary carcinomatous deposits.

Symptoms of tuberculous lymphadenitis:[25]

1. Painless, slowly progressive swelling
2. Weight loss
3. Temperature elevation
4. Anorexia
5. Fatigue
6. Malaise
7. Pain
8. Ulcer or sinus(if chronic)

Tuberculosis of bone:

Bone and joint tuberculosis accounts for up to 35% of all extrapulmonary tuberculosis. Skeletal tuberculosis is most common in the spine, followed by tuberculous arthritis of hip and knee and extraspinal tuberculous osteomyelitis.[15]

Tuberculosis of the spine was first described by Sir Percival Pott in 1782, and hence spinal tuberculosis is called Pott's spine.[26] Spinal TB accounts for 50% of the cases of skeletal TB.

Pott's disease most commonly involves thoracic spine. Intervertebral disc involvement from antero-inferior part of vertebral body results in anterior wedging and disc space obliteration causing gibbus.(palpable spinal prominence). Spinal involvement is due to hematogenous spread of Mycobacterium tuberculosis to the cancellous bone of the vertebral bodies. The site of primary infection is usally a pulmonary or genitourinary infection

The common presenting symptoms includes local pain, constitutional symptoms and paraplegia secondary to cord compression. The most common symptom is back pain localised to the site of disease most commonly in the thoracic region. The intensity of pain varies among different persons from mild dull aching pain to severe excruciating pain. The pain may be aggravated by movements of the spine, weight bearing and coughing.

In skeletal tuberculosis, arthrocentesis and synovial fluid mycobacterial cultures, synovial biopsy and bone biopsy for mycobacterial culture and histopathological examination are diagnostic investigations.[27]

The pathological changes[28] in the spine includes,

1. Central type of vertebral body involvement
2. Para-discal lesion
3. Anterior type of involvement of vertebral bodies

Dr.Prabakar et al.,in their study in 1989 comparing ambulatory treatment with chemotherapy and radical surgery with chemotherapy concluded that operative intervention is not needed in the great majority of patients and reported a favourable status of 97% at three years with nine months chemotherapy with isoniazid and rifampicin. Over the years the indications for surgery in tuberculosis spine has evolved.[29]

Paraplegia is the most common indication for surgical intervention in Pott's spine.

The other indications includes the following:[30]

Indications for surgery without neurological involvement

Progressive bone destruction in spite of ATT
Failure to respond to conservative therapy
Evacuation of paravertebral abscess when it has increased in size despite medical treatment
Uncertainty of diagnosis, for biopsy
Mechanical reasons:spinal instability caused by destruction or collapse, destruction of two or more vertebrae, kyphosis
Prevention of severe kyphosis in young children with extensive dorsal lesions
Large paraspinal abscess

Indications for surgery with neurological involvement[30]

New or worsening neural complications or lack of improvement with conservative treatment
Late onset paraplegia
Neural arch disease
Spinal tumor syndrome(epidural spinal tuberculoma without osseous involvement)

Causes of early onset paraplegia in Pott's spine:[30]

Mechanical pressure	Mechanical pressure by tuberculous debris, sequestrum of bone or disc, abscess, subluxation and dislocations, concertina collapse and internal gibbus.
Tuberculous granuloma	Tuberculoma in extradural, intradural, or intramedullary regions.
Tuberculous myelitis	Uncommon. May involve spinal cord parenchyma.
Spinal artery thrombosis	Infective thrombosis of spinal artery
Tuberculous arachnoiditis	Meningeal inflammation and fibrosis

Causes of late onset paraplegia in Pott's spine:[30]

Transection of spinal cord by bony bridge	Transverse ridge of bone produced by severe kyphosis.
Fibrosis of dura(pachymeningitis)	Formation of tough, fibrous membrane encircling the cord.

Litao Li et al., analysed retrospectively 35 cases of drug resistant spinal tuberculosis. 12 out of the 35 cases were multi drug resistant(MDR) and 23 did not meet the criteria for multi drug resistance. They reported that 33 out of the 35 cases were cured following surgery and chemotherapy guided by results of drug susceptibility testing(DST) and remained disease free at final follow up.(nearly 3 years follow up was done)[31]

Lan Xu et al, analysed 19 patients of drug resistant spinal tuberculosis of which 16 patients had multidrug resistant tuberculosis and 3 patients had non multi drug resistant tuberculosis. They reported that all of their study population were cured following surgical intervention(open surgery and percutaneous drainage with local chemotherapy) and remained disease free at final followup(2 years)[32]

Laboratory Diagnosis:

The diagnostic challenges in extrapulmonary tuberculosis includes lack of adequate amount or volume of samples, the samples being divided into portions for several diagnostic tests(histology, cytology, biochemistry, microbiology) resulting in non uniform distribution of organisms and the paucibacillary nature of the disease.[33]

Histopathological Examination:

Granuloma is a focal collection of inflammatory cells in a compact manner in which mononuclear cells predominate. Granuloma is the histological hallmark of tuberculosis and tuberculosis is described as the proto type of granulomatous inflammation. Granulomas contain the spread of infection by the active involvement of numerous enzymes and cytokines. Granulomas are the result of delayed type hypersensitivity or persistent organisms.

The granulomas seen in active tuberculosis are soft or exudative granulomas which contain acid fast bacill and are not well circumscribed,

whereas the granulomas seen in healed tuberculosis are hard or proliferative granulomas which are well circumscribed and usually do not contain acid fast bacilli.

The various etiological agents for granulomatous response includes:

Mycobacteria	Tuberculosis, leprosy, Buruli ulcer, swimming pool granuloma
Bacteria	Brucellosis, meliodosis, actinomycosis, nocardiosis,granuloma inguinale,listeriosis, tularaemia
Chlamydiae	Lymphogranuloma venereum, trachoma
Rickettsiae	Q fever
Spirochetes	Syphilis, pinta, yaws
Fungi	Cryptococcosis, candidiasis, sporotrichosis,histoplasmosis, aspergillosis, blastomycosis,coccidiodomycosis, chromoblastomycosis, mycetoma
Protozoa	Leishmaniasis, toxoplasmosis
Nematodes	Visceral larva migrans
Trematodes	Schistosomiasis, paragonimiasis,fascioliasis,clonorchiasis
Viruses	Infectious mononucleosis,cytomegalovirus, measles,mumps
Foreign body	Talc,silica
Bacterium	Cat scratch disease

Microbiological examination:

The lack of diagnostic gold standard makes the situation complex. The various diagnostic modalities for demonstration for organisms includes smear for acid fast bacillus, culture methods and molecular analysis.

The processing of extra-pulmonary specimens require milder decontamination methods since they are paucibacillary. It is necessary to inoculate onto multiple media such as LJ, LJ slopes, SK medium enriched with sodium pyruvate (SP) to get better culture yield.[34]

The lack of gold standard for diagnosis for extrapulmonary tuberculosis is striking in the metaanalysis comparing various diagnostic standards against Xpert MTB/RIF by Stephen D Lawn et al,[35]

Torticoli et al., in 2012 in their study in Italy[37] used

1. culture(both solid and liquid) or
2. suggestive radiology/histology with documented positive response to tuberculosis treatment as gold standard.

Armand et al., in 2011[38] from France used culture in both solid and liquid media as gold standard.(n=32)

Causse et al., from Spain in 2011[39] included tissue biopsies, CSF, gastric aspirates, pleural fluid, purulent exudates in their analysis and used solid and liquid media culture as gold standard.(n=41)

Friedrich et al., from South Africa in 2011[40] used liquid culture as gold standard in their analysis.

Hillemann et al., from Germany in 2011[41] used solid and liquid culture as gold standard for tuberculosis diagnosis in samples of tissue, gastric aspirate and urine in their analysis.

Ligthelm et al., from South Africa in 2011[42] used a composite gold standard of

1. positive cytology + AFB and/or
2. Culture of MTB

Moure et al., from Spain[43] in their analysis of lymph node, abscess aspirates, lymph nodes and pleural fluid used solid and liquid culture as the gold standard.

In India, Vadwai et al, in 2011[44] used a composite gold standard of

1. Smear
2. Culture
3. Clinical
4. Radiology and
5. Histology

In another study by A K Maurya et al., in 2012 used BACTEC culture as the gold standard in their analysis of samples from multiple extra pulmonary sites.[36]

In the studies which used solid and liquid culture as the sole gold standard criterion for diagnosis have a lower positivity rate. And the ideal gold standard would be a combination of clinical, microbiological and clinical response to tuberculosis treatment in follow up.

The atypical clinical presentation, wide differential diagnosis and difficulty in procuring adequate representative sample for microbiological and histopathological examination and lack of uniform diagnostic criteria has been a hurdle in prompt diagnosis of disease and huge variation in epidemiological data from different regions of the world.

A K Maurya et al., in 2012[36] reported patterns of drug resistance in extra pulmonary tuberculosis in North India. In their study they included 756 patients with clinical diagnosis of extra pulmonary tuberculosis of various sites including lymph node tuberculosis, cold abscess, pleural fluid, genitourinary tuberculosis, ascitic fluid, biopsy materials, pus, pericardial fluid, synovial fluid and bone marrow aspirates. Of the clinical suspects of extra pulmonary tuberculosis 30.1%(n=165) were positive for mycobacteria by BACTEC culture. They included only the culture positive cases for further analysis. 74.5% of their study population were new patients(no treatment or less than one month of treatment against tubercle bacilli) and 25.5% had previous

history of treatment, history of contact was present in 25.4% of patients,11.5% patients were having a history of diabetes mellitus and 1.8% of cases were HIV positive.

They subjected the culture isolates for drug susceptibility testing for first line anti-tuberculous drugs including isoniazid, rifampicin, ethambutol and streptomycin. They observed higher presence of resistant strains in patients with history of prior treatment with antituberculous drugs. 61.8% of new cases were susceptible to all drugs and 57.2% of previously treated cases were susceptible to all drugs. They observed that monoresistance and resistance to two drugs were more common in new cases whereas resistance to three drugs and resistance to four drugs were more common in previously treated cases. They observed that on the whole 39.9% of extrapulmonary tuberculosis cases were resistant to first line anti-tubercular drugs.

Among the resistant cases, they found multi drug resistant tuberculosis(MDR-TB) to be present in 13.5% of cases of extrapulmonary tuberculosis. They considered that the reason for this high rate of multi drug resistant tuberculosis(MDR-TB) could be due to the fact that chronic cases with high suspicion of drug resistance were subjected to drug susceptibility testing (DST) in their tertiary care hospital.

AIMS OF THE STUDY

1. To study the clinical data and histopathological correlates in clinical suspects of lymph node and bone tuberculosis.
2. To study the microbiological pattern in clinically suspected cases of lymph node and bone tuberculosis.
3. To study the pattern of drug resistance in microbiologically confirmed cases of lymph node and bone tuberculosis.

MATERIALS AND METHODS

Study design: Prospective Observational Study.

Study Period: March 2014 – August 2014.

Inclusion criteria:

1. Patients clinically suspected as lymph node/bone tuberculosis in whom treating doctor has suggested surgical intervention for histopathological/microbiological diagnosis/therapeutic reasons in Thoracic Medicine/General Surgery/Orthopaedics departments at Rajiv Gandhi Government General Hospital, Chennai.
2. Patient with/without history of previous anti-tuberculous treatment.
3. Patients seropositive/seronegative for human immunodeficiency virus.
4. Patients with/without pulmonary tuberculosis.
5. Patients willing to participate in the study.

Exclusion Criteria:

1. Patients clinically suspected as lymph node/bone tuberculosis in whom the treating doctor has not suggested histopathological/microbiological diagnosis/therapeutic interventions.
2. Patients currently on anti tuberculous therapy for more than 2 weeks.
3. Patients not willing to participate in the study.

Sample Size :

114 patients who attended outpatient department of Thoracic Medicine/General Surgery/Orthopaedic departments of Rajiv Gandhi Government General Hospital satisfying inclusion/exclusion criteria were enrolled in the study.

Methodology:

84 consecutive patients who presented with lymph node enlargement in superficial lymph node groups (cervical/axillary/inguinal) and suspected as lymph node tuberculosis by the treating doctor and were referred for surgical excision for diagnostic/therapeutic reasons were included in the study.

31 consecutive patients who presented with clinical and radiological features consistent with tuberculous spodylitis and surgical management suggested by treating doctor for diagnostic/therapeutic reasons were included in the study.

The patients included in the study were admitted in the hospital after explaining about the study in detail and obtaining informed consent. Detailed clinical history including

1. Presenting complaints
2. Duration of symptoms
3. History of constitutional symptoms

4. History of contact with sputum positive case of tuberculosis
5. Previous history of treatment for tuberculosis/ history of diabetes mellitus and other comorbid illness was obtained.

General examination and structured clinical examination were done as relevant for the case.

Routine investigations including

1. Chest X ray PA view
2. Hemogram
3. Random Blood Sugar
4. HIV antibody testing were done for all patients.

Other investigations including

- Fasting Blood Sugar
- Postprandial Blood Sugar
- Renal Function Test
- Liver Function Test
- Sputum for Acid Fast Bacilli
- Ultrasonogram Abdomen/Neck
- X ray Lumbo sacral/dorsal spine
- MRI Spine were done as warranted by clinical situation.

Pre operative evaluation was done and patients were posted for surgery after obtaining anaesthetic fitness. Cardiology clearance was obtained in patients greater than 40 years of age.

In lymph node tuberculosis suspects, excision of lymph nodes was done under local/general anaesthesia. Skin crease incision was made and lymph nodes excised in toto. The sample was divided into two. One portion was sent in formalin container to the pathology lab. The other portion was sent in Kirschner's medium to National Reference Labarotory, National Institute for Research in Tuberculosis (NIRT), Chetpet, Chennai on the same day of surgery for direct smear examination for AFB, Lowenstein-Jensen (LJ) culture and Drug Susceptibility Testing (DST).

In bone tuberculosis suspects, pus, bone debris specimens from site of pathology were divided into two. One portion was sent for histopathological examination and the other portion sent to NIRT for direct smear examination for AFB, LJ culture and DST.

Extra pulmonary specimens in general are paucibacillary in nature and hence their processing methods require milder decontamination. Hence the specimens are inoculated into media made selective by incorporating polymyxin B, amphotericin B, carbenicillin, vancomycin and trimethoprim to inhibit growth of other microorganisms (PACT).

The tissue specimens are cut into small pieces using sterile scissors and transferred into a sterile tissue grinder tube and homogenised with 5 ml of

sterile water. A direct smear is made from the homogenate. The smear is prepared and read using modified Ziehl-Neelson method.

The homogenate is centrifuged for 15 minutes and the supernatant decanted. 5% sulphuric acid solution is added to the deposit and centrifuged at 3500 rpm for 15 minutes. After discarding the supernatant the deposit is mixed with 0.2 ml sterile water and inoculated onto two slopes of Lowenstein – Jensen media and incubated at 37 degree Celsius.

The cultures are read weekly and typical colonies of Mycobacterium tuberculosis are rough, buff, tough, nonpigmented (cream coloured) and slow-growers i.e. Colonies appearing after one or two weeks after inoculation.

Niacin test, inhibition by paranitrobenzoate and catalase test are done for species identification. Mycobacterium tuberculosis yield positive niacin test (pink colour), positive catalase test (bubbles seen) and inhibited by paranitrobenzoate (PNB).

Drug susceptibility is tested by 1% proportion method. Resistance is defined as mycobacteria with greater than 1% of the population exhibiting growth in the presence of the lowest concentration of drug tested.[34]

In this method suspension of growth is prepared by scrapping representative sample into 0.3 ml of sterile distilled water and a uniform suspension made and kept aside for coarser particles to settle down. Serial

dilutions are made from this suspension by adding 0.2 to 1.8 ml of sterile water [$10^{-1}(S_1)$,$10^{-2}(S_2)$,$10^{-3}(S_3)$..]

Concentrations of drugs used in drug susceptibility testing (DST):

Dihydrostreptomycin	:	4 µg/ml
Isoniazid	:	0. 2 µg/ml
Rifampicin	:	40 µg/ml
Ethambutol	:	2 µg/ml

The results were interpreted based on 42-day readings. If there was clear-cut resistance based on the 28-day reading the results are reported as such. Strains susceptible at 28 days were read again at 42 days and reported based on the later reading only.

Dilution	Drug-free	$H_{0.2}$
S_1	3+ (1700)	2+
S_2	3+ (170)	2+
S_3	16, 18 (17)	18
S_4	1, 2	7
% Res: 18/17 = 105. 9% = 100% R		

Dilution	Drug-free	SM_4
S_1	3+ (2400)	-*
S_2	* (240)	-
S_3	21, 27 (24)	-
S_4	1, 4	-
% Res: 1/2400 = 0. 04 % S		
* Calculate assuming a growth of 1 colony		

Dilution	Drug-free	Emb_2
S_1	3+ (7200)	2+
S_2	3+ (720)	65
S_3	76, 68 (72)	3
S_4	3, 6	1
% Res: 65/720 = 9. 0% R		

Dilution	Drug-free	Emb_2
S_1	3+ (8500)	22
S_2	3+ (850)	2
S_3	82, 88 (85)	-
S_4	3, 2	-
% Res: 22/8500 = 0. 26% S		

Figure 1: Illustration of 1% proportion method

The colonies growing on drug containing medium inoculated with the 10^{-1} dilution that equal or more the number of colonies growing on the control medium (drug free medium) inoculated with the 10^{-3} dilution suggests 1% or more of the test population. If the calculation was 1% or more then results interpreted as resistance[34].

Definitions:

1. H/O contact:

   A person exposed to *M. tuberculosis* infection by sharing air space with a case of sputum positive pulmonary tuberculosis at household or workspace.

2. Anemia:

   Anemia is defined as haemoglobin concentration less than 13 grams/decilitre in males and less than 12 grams/decilitre in females.

3. Elevated Erythrocyte Sedimentation Rate(ESR):

   ESR greater than 40 mm per hour is defined as high ESR.

4. Constitutional symptoms:

   History of fever, loss of appetite, loss of weight(as perceived and reported by the patient) of more than two weeks duration.

5. Diabetes mellitus:

   Fasting blood sugar greater than 126 mg/decilitre and/or random blood glucose greater than 200 mg/decilitre.

6. Case of lymph node/bone tuberculosis:

A patient is defined as having lymph node/ bone tuberculosis if either granulomas are present in histopatology or LJ culture shows growth and identified as Mycobacterium tuberculosis or both.

7. New case:

A new case of lymph node/bone tuberculosis is defined as a patient of lymph node/bone tuberculosis who has not received anti tuberculosis drugs previously or taken anti tuberculosis drugs of less than 4 weeks duration.

8. Previously treated case:

A previously treated case of lymph node/bone tuberculosis is defined as a patient of lymph node/bone tuberculosis who has received more than 4 weeks of anti tuberculous drugs.

9. HIV:

A patient is defined as HIV seropositive if he/she tests positive by rapid HIV antibody test and confirmed by a second antibody test.

10. Granuloma

The granuloma consists of blood-derived macrophages, epithelioid cells and Langhans giant cells surrounded by T lymphocytes with or without necrotic centers.

11. Smear positive for AFB:

Direct smears prepared after homegenisation of the sample were processed using modified Ziehl-Neelson technique and reported as positive according to WHO grading scale.

12. Culture positive for Mycobacterium tuberculosis:

Homogenised specimen inoculated on Lowenstein-Jensen slopes and reported as positive and identified as Mycobacterium tuberculosis by biochemical tests.

13. Resistance to first line antituberculous drug:

The subcultures inoculated on drug free and drug containing media in suspensions of serial dilutions and reported as resistant by 1% proportion method.

Statistical analysis:

Statistical analysis was done using the SPSS software. Significance of correlation between variables was assessed using p value. A correlation was considered to be statistically significant if its p value is less than 0.05.

OBSERVATION AND RESULTS

We diagnosed lymph node tuberculosis and bone tuberculosis if either granulomas were present in histopathology or LJ culture showed growth and identified as mycobacterium tuberculosis or both.

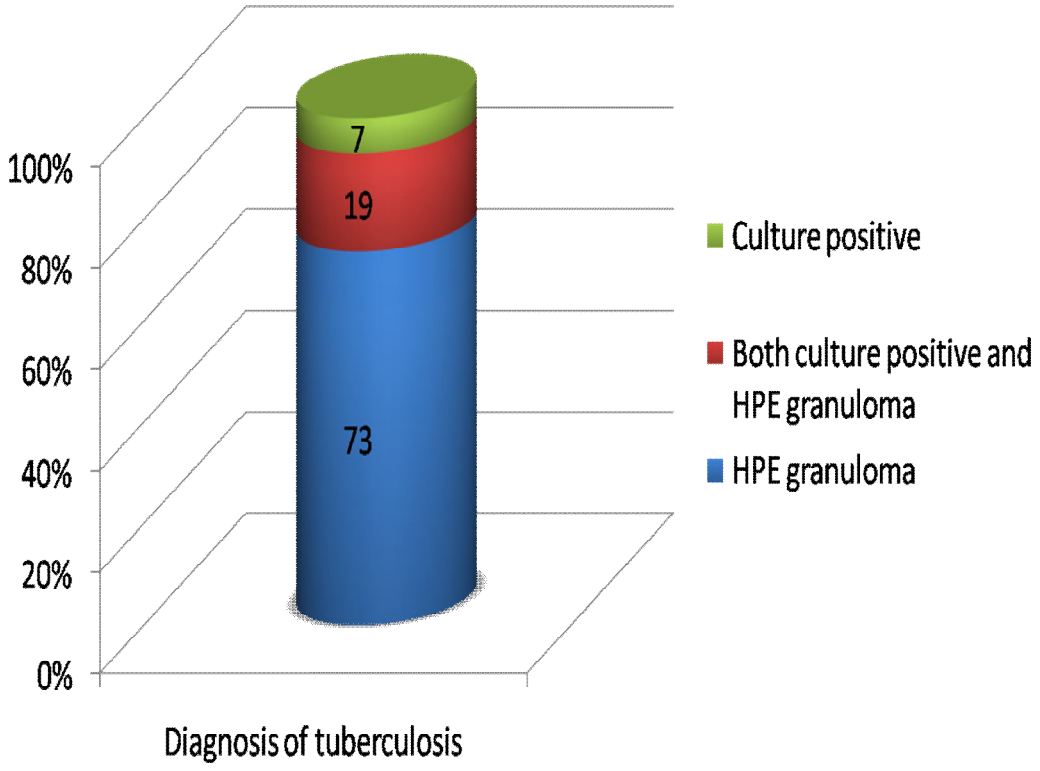

Figure 2 – Diagnosis of lymph node tuberculosis and bone tuberculosis.

We diagnosed 19 cases as tuberculous based on both granulomas in histopathology and growth in LJ medium identified as Mycobacterium tuberculosis, 73 cases based on granulomas in histopathology alone and 7 cases based on LJ culture alone.

Out of 114 clinical suspects of lymph node and bone tuberculosis, 99 were diagnosed as tuberculous, lymph node(n=74) and bone(n=25).

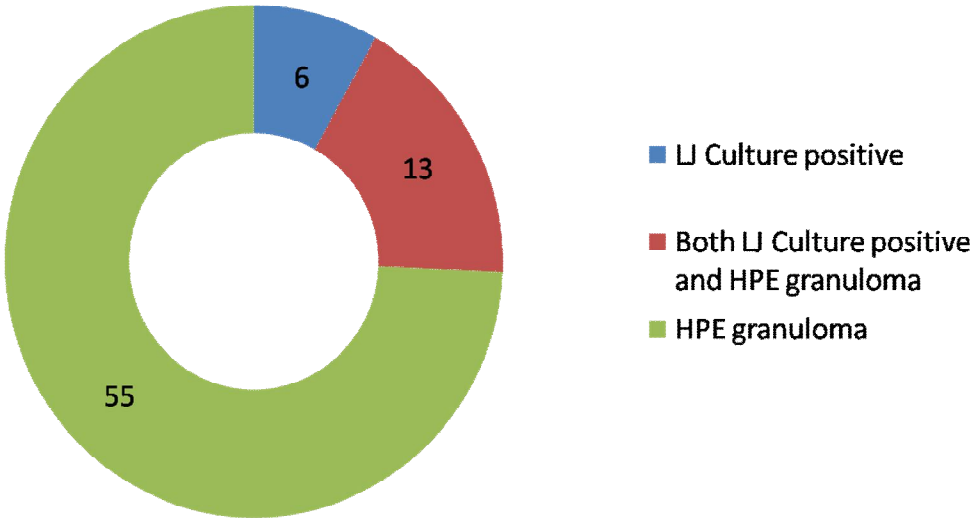

Figure 3 : Diagnosis of lymph node tuberculosis

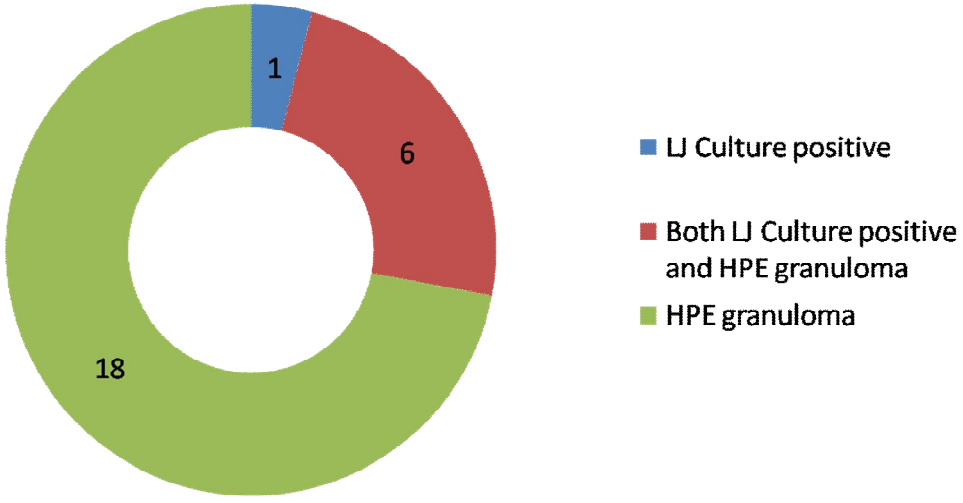

Figure 4: Diagnosis of bone tuberculosis

Our study included 114 patients of clinical suspects of lymph node (n=83) and bone tuberculosis (n= 31).

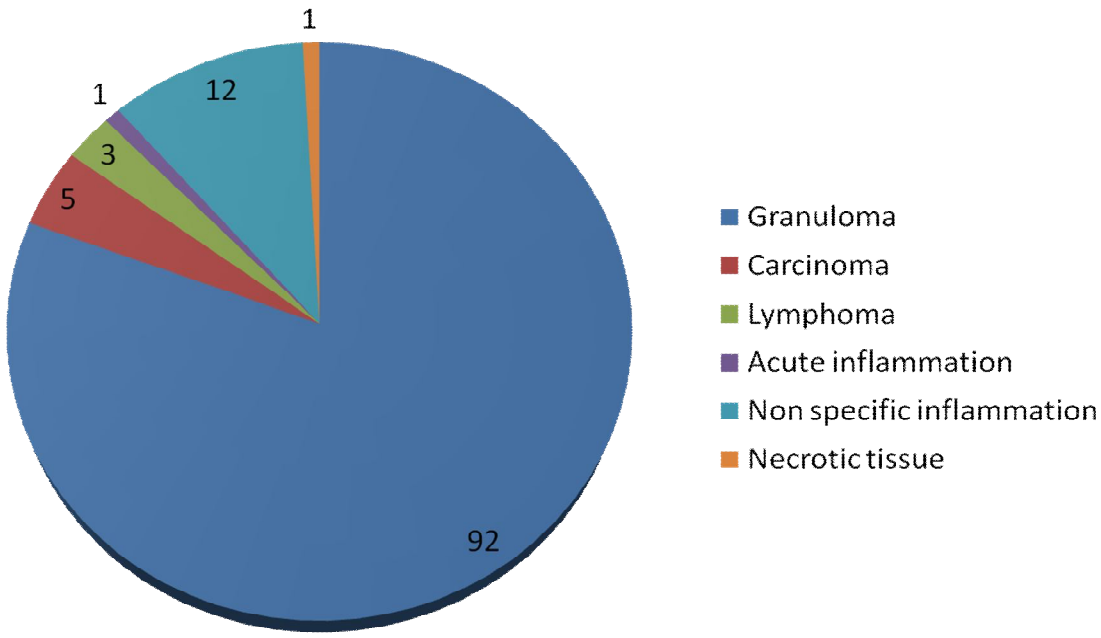

Figure 5– Histopathological patterns in clinical suspects of lymph node and bone tuberculosis.

Out of the 114 patients 92 patients had granulomas , 12 patients had non specific inflammation, 5 patients had carcinoma, 3 patients had lymphoma, 1 patient had acute inflammation and 1 patient had necrotic tissue on histopathological examination of the biopsy specimens.

We observed that LJ culture showed growth and isolates identified as Mycobacterium tuberculosis in 26 cases out of 114 cases.

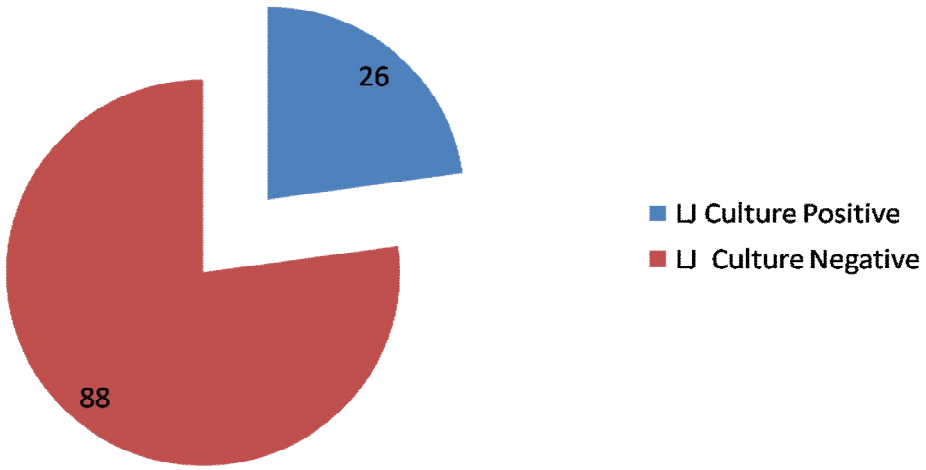

Figure 6 – LJ culture showing growth of Mycobacterium tuberculosis.

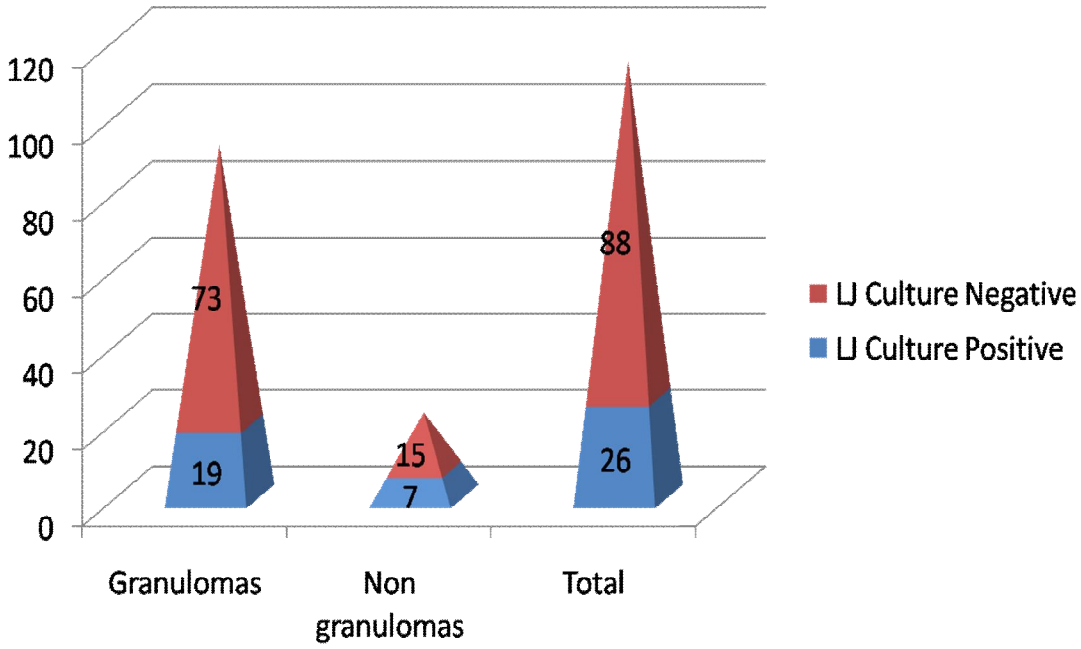

Figure 7 – Comparison of histopathological pattern and AFB culture.

Out of 92 patients with granulomas on histopathology 19 were positive in LJ culture and out of 22 patients with non granulomas on histopathology 7 were positive in LJ culture.

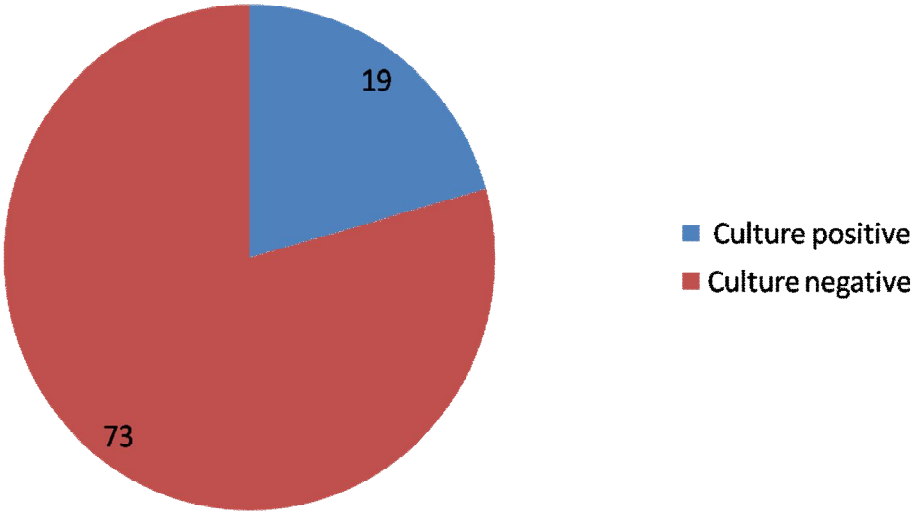

Figure 8: HPE Granuloma

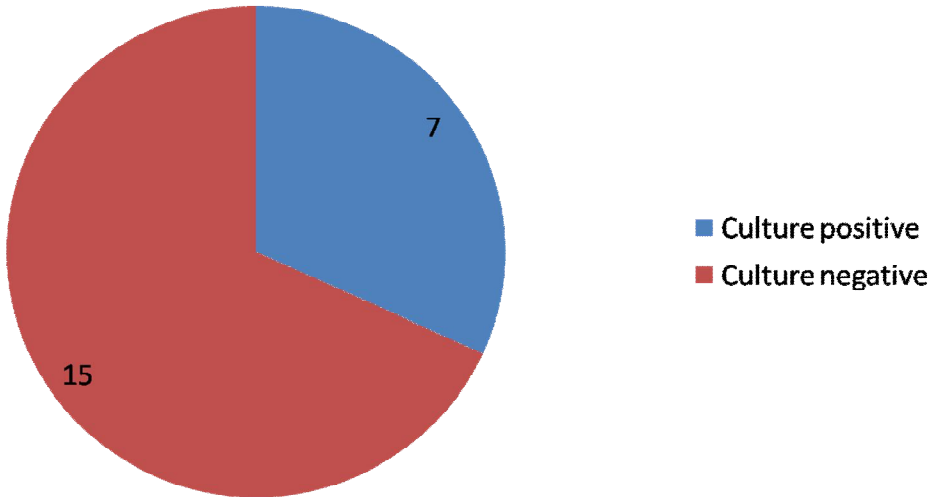

Figure 9:HPE non granuloma

Supportive evidence in lymph node and bone tuberculosis versus other diagnosis

Supportive Evidence	Contact History present	Contact History absent	Constitutional Symptoms present	Constitutional Symptoms absent	Anemia present	Anemia absent	ESR > 40 mm/hour	ESR ≤ 40 mm/hour
Tuberculosis	24	75	80	10	60	39	85	14
Other diagnosis	3	12	12	3	9	6	13	2

Table 1 : Supportive evidence in tuberculous versus other diagnosis

We analysed the contributions of contact history, constitutional symptoms, anemia and elevated ESR in the clinical suspicion of lymph node and bone tuberculosis.

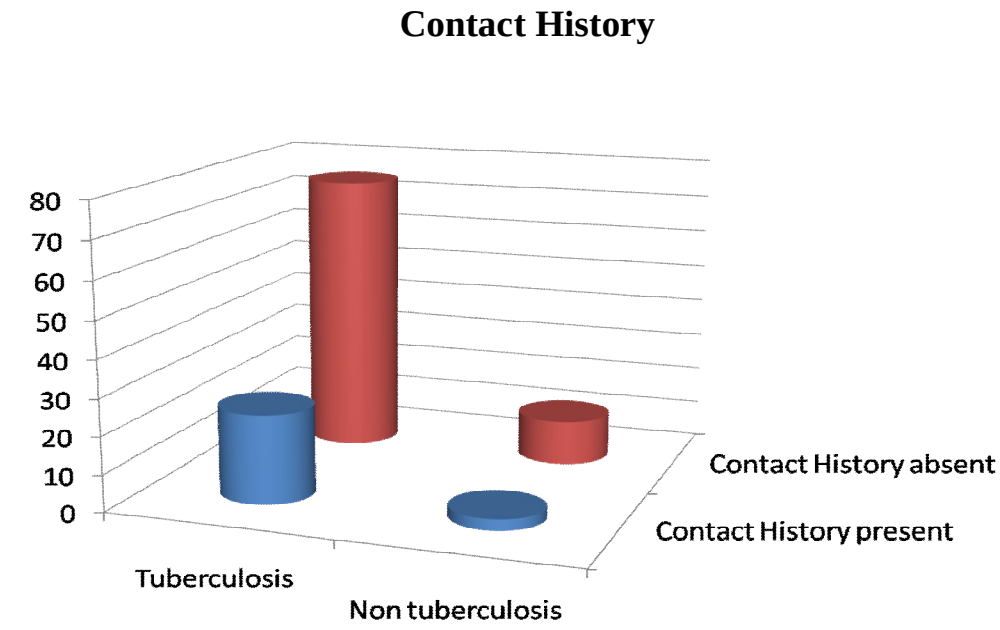

Figure 10: History of contact in tuberculous versus other etiologies

History of contact was present in 24 % of patients with tuberculosis.

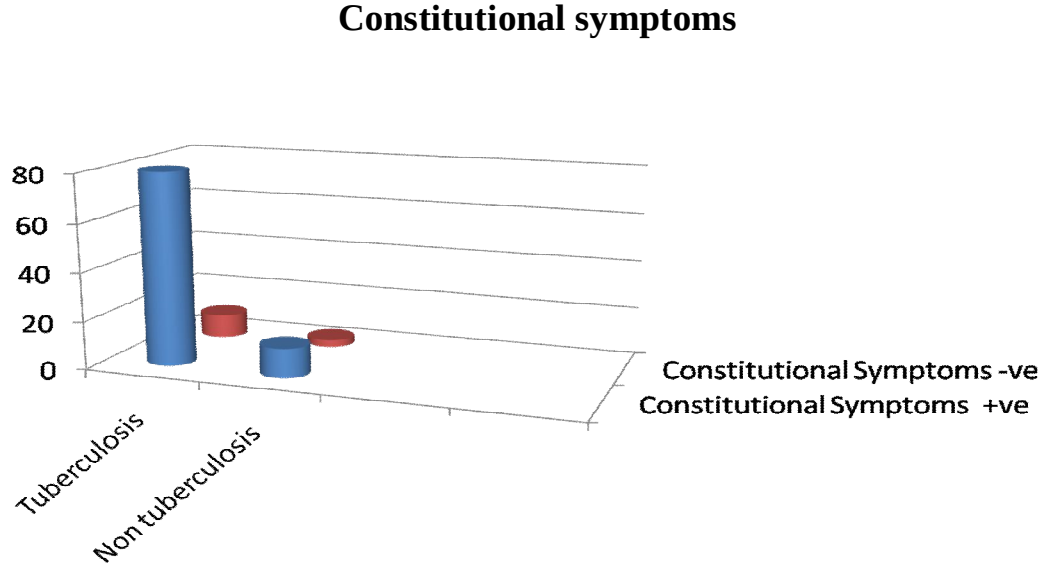

Figure 11: Constitutional symptoms in tuberculosis versus other etiologies

Constitutional symptoms were present in 81% of patients with tuberculosis.

Anemia

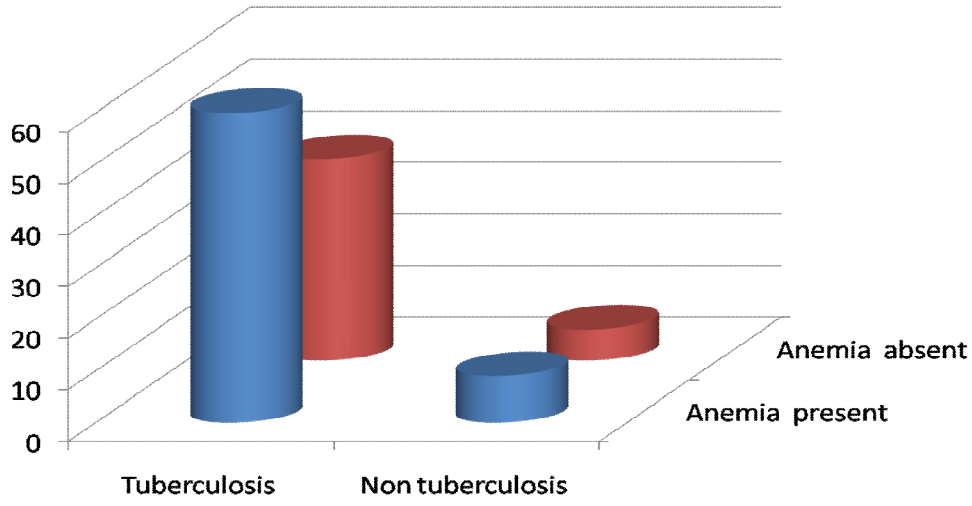

Figure 12: Anemia in tuberculosis versus other etiologies

Anemia was present in 60% of patients with tuberculosis.

Elevated ESR

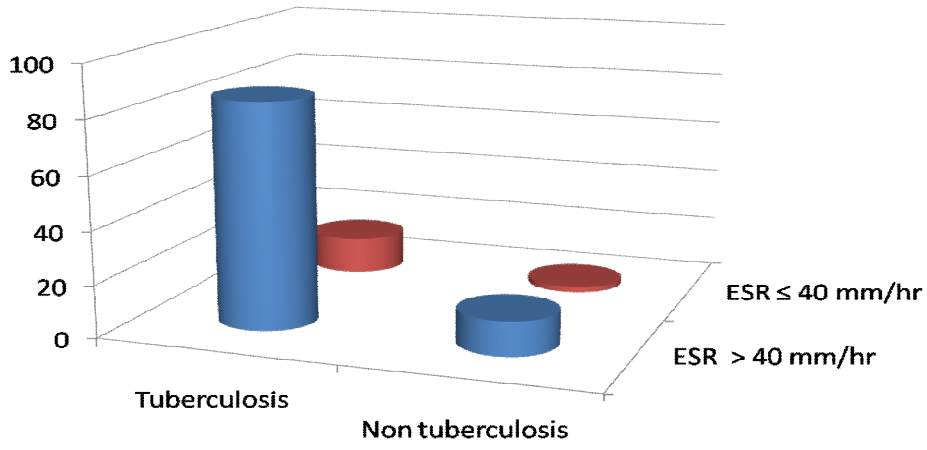

Figure 13: Elevated ESR in tuberculosis versus other etiologies

Elevated ESR was present in 86% of patients with tuberculosis.

Supportive evidence in diagnosis of lymph node and bone tuberculosis

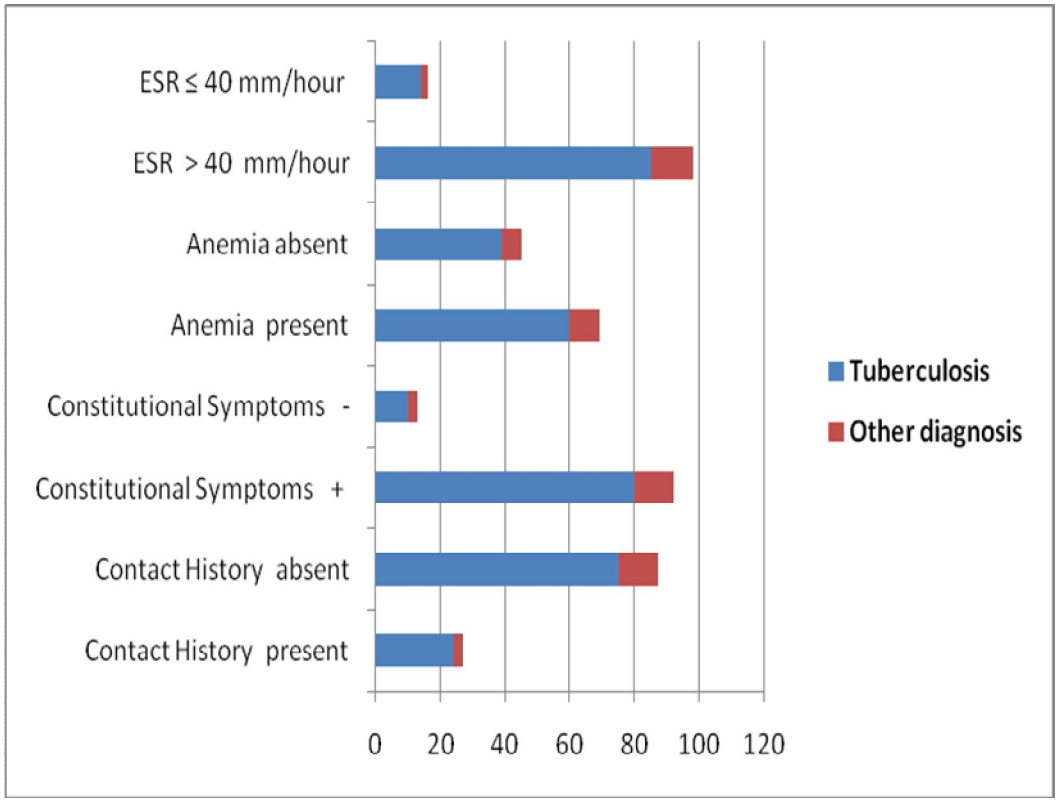

Figure 14: Role of supportive evidence in diagnosis of tuberculosis

We observed that history of contact was present in 24 % of patients with tuberculosis and 20% of patients with non tuberculous etiology. We observed that constitutional symptoms were present in 81% of patients with tuberculosis and 80% of patients with other etiologies.

We observed that anemia was present in 60 % of patients with tuberculosis and 60 % of patients with other etiologies and elevated ESR in 86 % of patients with tuberculosis and 87 % of patients with other diagnosis.

Age distribution

Age Distribution - Lymph Node Vs Bone TB	Lymph Node TB	%	Bone TB	%
11-20 Years	35	47.29	0	0
21-30 Years	30	40.5	8	32
31-40 Years	1	1.35	10	40
41-50 Years	2	2.70	4	16
51-60 Years	6	8.10	2	8
61-70 Years	0	0	1	4
Total	74	100	25	100

Table 2 – Age distribution in lymph node and bone tuberculosis

The peak age distribution observed in lymph node tuberculosis is 11 -20 years (47.29%), closely followed by 21-30 years (40.5%). These two age groups together constitute nearly 88% of cases of lymph node tuberculosis in our study.

The peak age distribution that we observed in bone tuberculosis is 31-40 years (40%), followed by 21-30 years (32%). These two age groups constitute 72% of cases of bone tuberculosis.

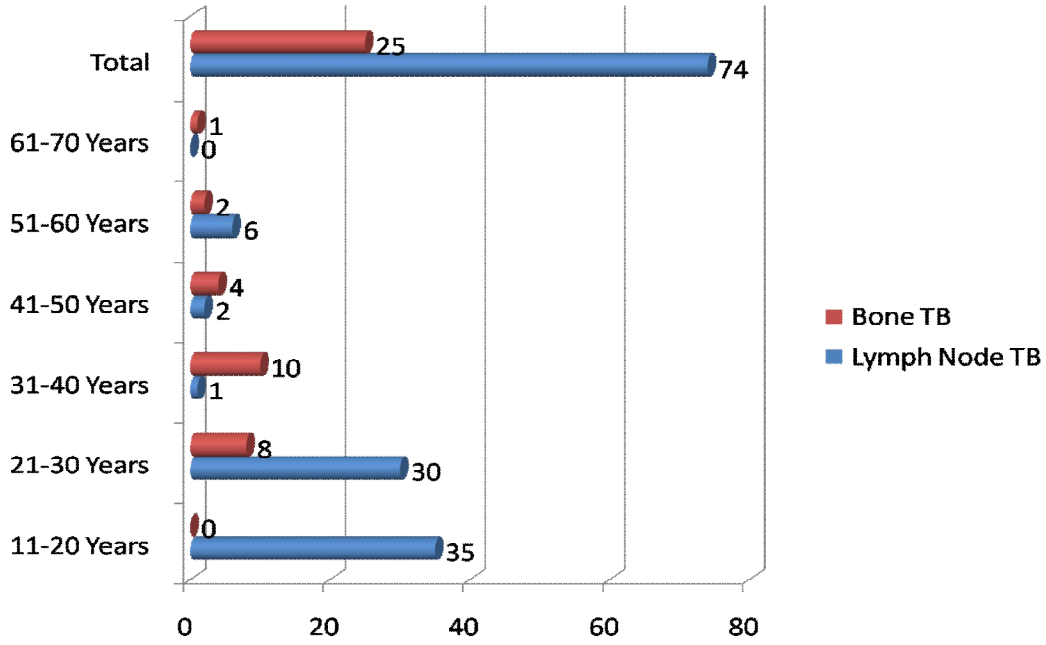

Figure – 15: Age distribution in lymph node and bone tuberculosis

Both lymph node and bone tuberculosis is relatively less common in age greater than 40 years. We observed that only 10% of lymph node tuberculosis occurs in age greater than 40 years and 24% of bone tuberculosis occurs in age greater than 40 years.

Age Distribution - Lymph Node Vs Bone TB	Lymph Node TB	Bone TB
N	74	25
Mean	25.06	35.26
SD	14.02	12.04
P value Unpaired t Test		0.000289

Table -3: Mean age in lymph node and bone tuberculosis

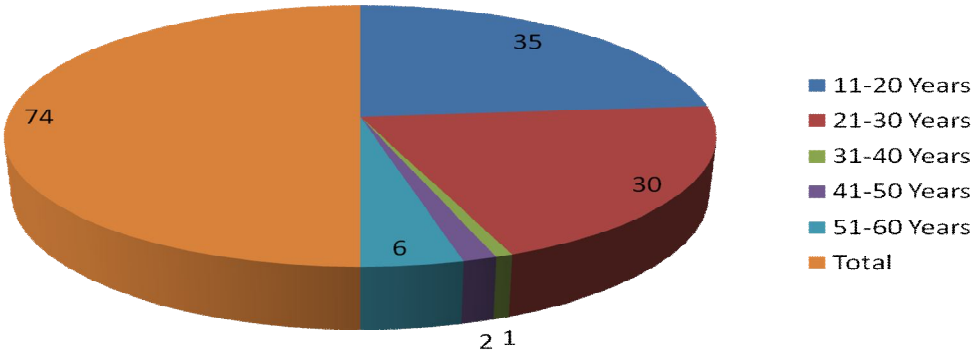

Figure 16– Lymph node tuberculosis age distribution

The mean age of occurrence of lymph node tuberculosis in our study is 25 years.

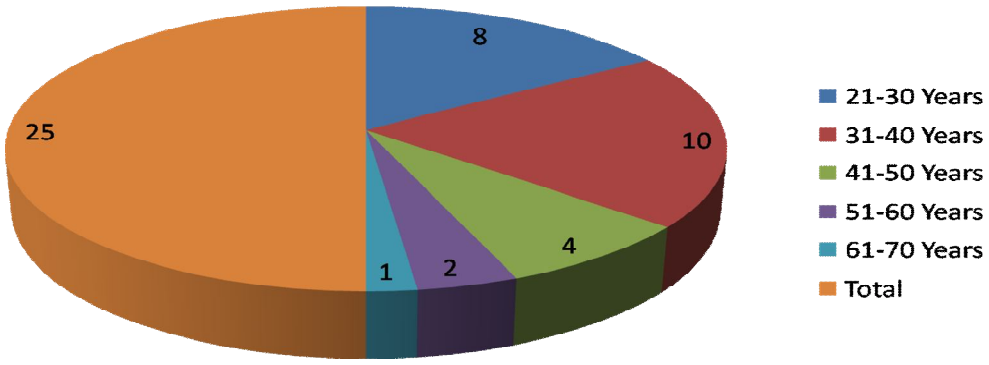

Figure 17– Bone tuberculosis age distribution

The mean age of occurrence of bone tuberculosis in our study is 35 years.

Gender distribution

Gender Distribution	Lymph Node TB	%	Bone TB	%
Male	27	36.48	15	60
Female	47	63.51	10	40
Total	74	100	25	100
P value Fishers Exact Test			0.011	

Table 4: Gender distribution in lymph node and bone tuberculosis.

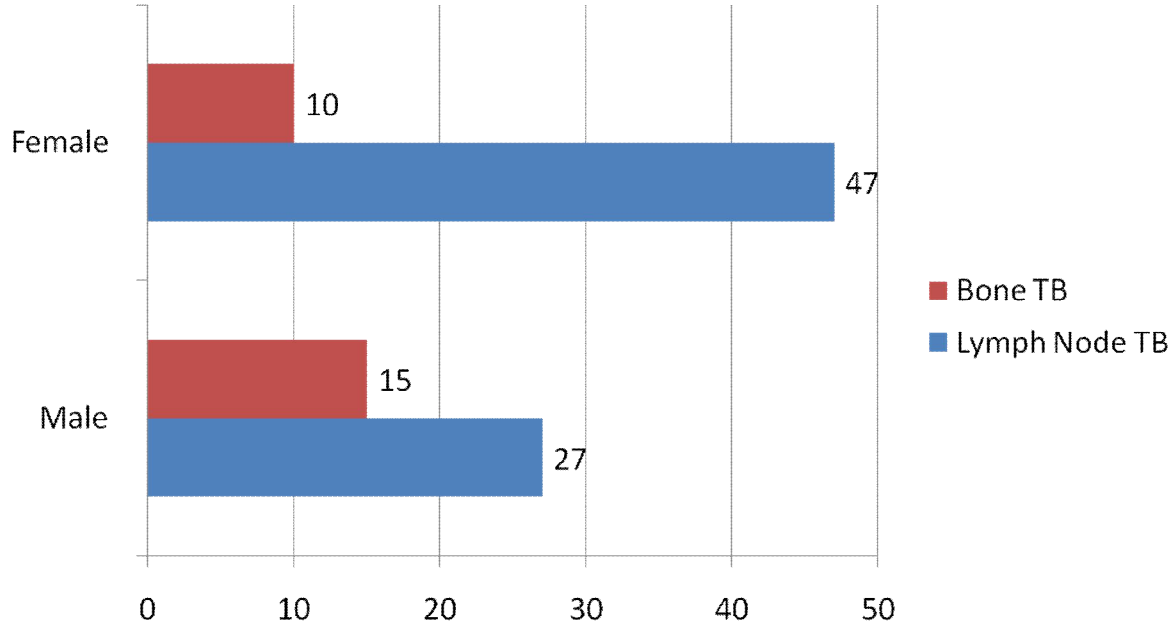

Figure 18: Gender distribution in lymph node and bone tuberculosis.

We observed a female preponderance in lymph node tuberculosis (63.51%) and male preponderance in bone tuberculosis (60%) which is statistically significant [p value -0.011]

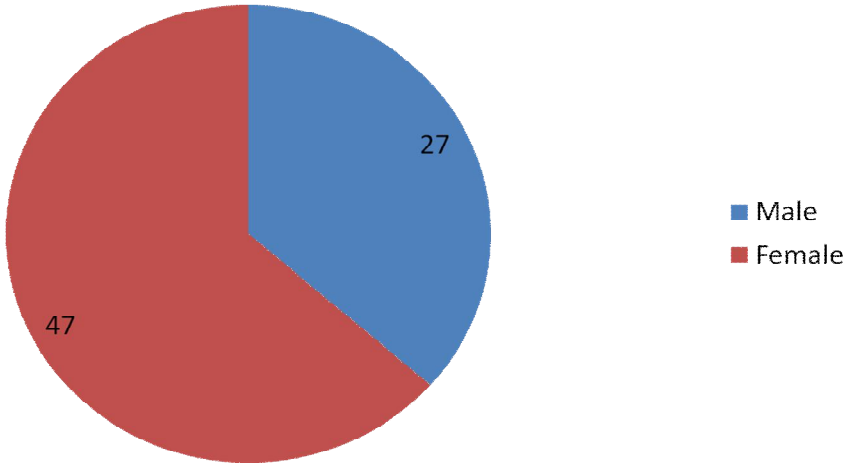

Figure 19: Gender distribution in lymph node tuberculosis

In our study the ratio of male : female patients in lymph node tuberculosis is 3 : 5.3.

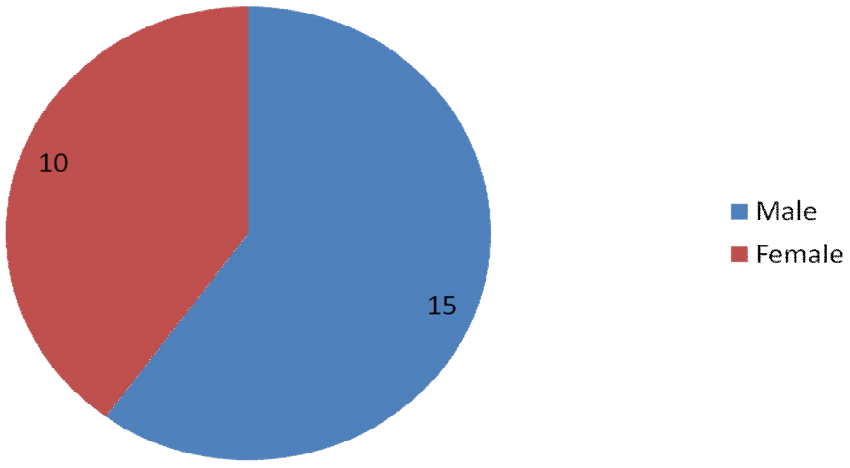

Figure 20 : Gender distribution in bone tuberculosis

We observed a male: female ratio of 3 : 2 in bone tuberculosis.

Sites of involvement in lymph node tuberculosis

Site of involvement	Number of cases
Anterior cervical	31
Posterior cervical	35
Submandibular	4
Axillary	3
Inguinal	1

Table 5 : Sites of involvement in lymph node tuberculosis

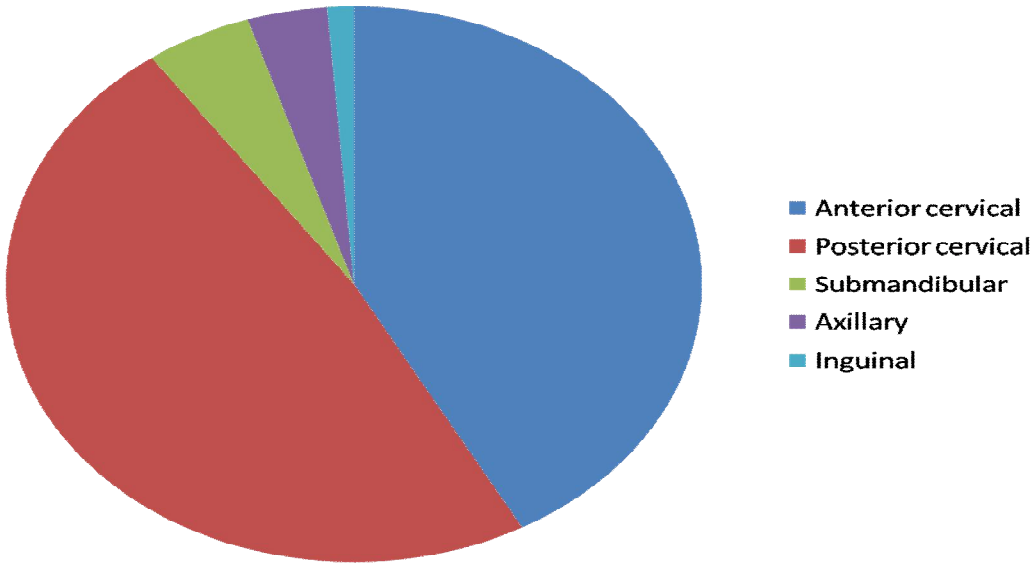

Figure 21: Lymph node tuberculosis-sites of involvement

In our study, we observed that posterior cervical lymph node involvement was seen in 35 cases, anterior cervical in 31 cases, submandibular in 4 cases, axillary in 3 cases and inguinal in 1 case.

Sites of involvement in bone tuberculosis

Site of disease	Number of cases
Upper thoracic disease(above D4)	1
Lower thoracic disease(below D4)	17
Lumbar disease	7

Table 6: Bone tuberculosis(spine) – sites of involvement

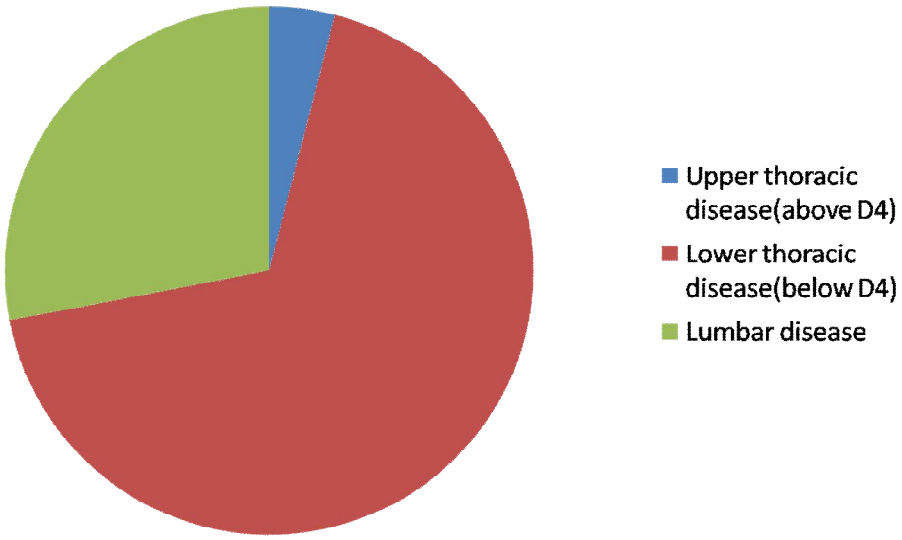

Figure 22: Spine tuberculosis – sites of involvements

We observed 17 cases of bone tuberculosis in lower thoracic spine, 6 cases in lumbar spine and 2 cases in thoracic spine.

Contact History

Contact History Status	New Cases	%	Previously Treated Cases	%
Contact History present	22	27.16	2	11.1
Contact History absent	59	72.83	16	88.88
Total	81	100	18	100
P value Fishers Exact Test			0.1513	

Table 7: History of contact with sputum positive pulmonary tuberculosis in new and previously treated patients

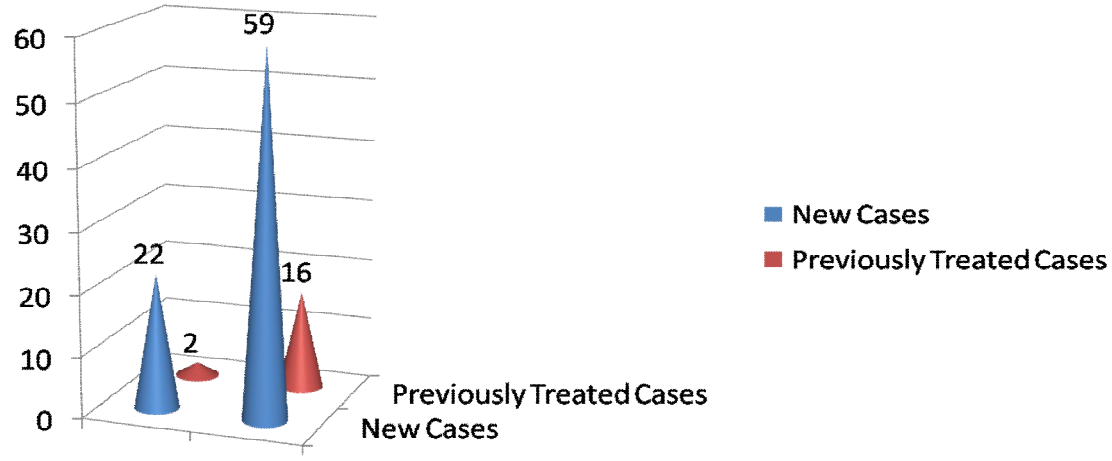

Figure 23: Contact History among new and previously treated patients

In our study we observed that 27% new patients and 11.1% previously treated patients had history of contact with sputum positive case of pulmonary tuberculosis.

Constitutional Symptoms

Constitutional Symptoms	New Cases	%	Previously Treated Cases	%
Constitutional Symptoms present	71	87.65	18	100
Constitutional Symptoms absent	10	12.34	0	0
Total	81	100	18	100
P value Fishers Exact Test			0.4594	

Table 8: Constitutional symptoms in new and previously treated patients

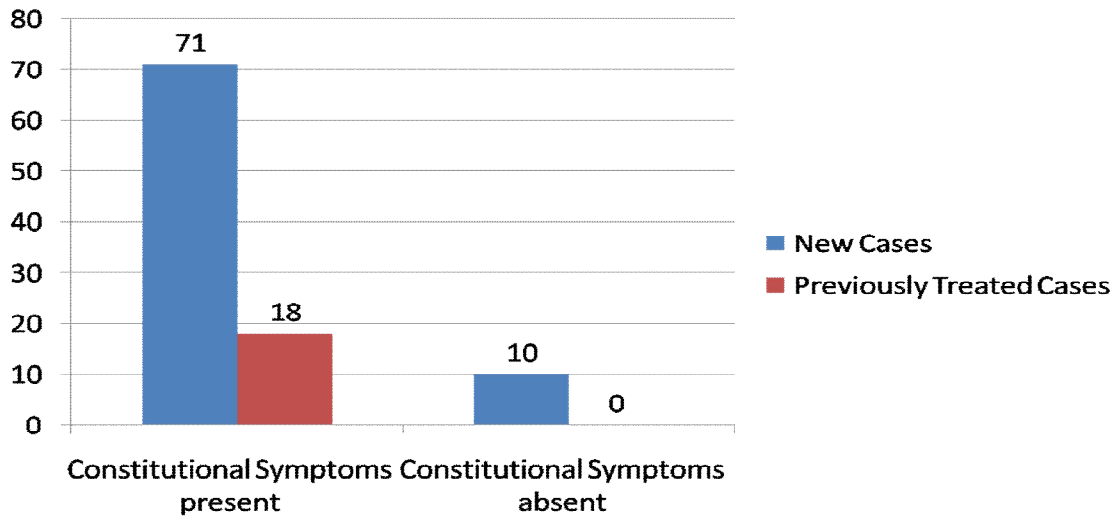

Figure 24: Constitutional symptoms in new and previously treated patients

We observed that constitutional symptoms were present in 71 out of 81 new patients(87.65%) of lymph node and bone tuberculosis and in all the previously treated patients.

Anemia

Anaemia Status	New Cases	%	Previously Treated Cases	%
Anaemic	49	60.49	11	61.11
Not Anaemic	32	39.50	7	38.88
Total	81	100	18	100
P value Chi Squared Test			0.6522	

Table 9: Anemia(Hb<13 g/dl in males and Hb<12 g/dl in females) in new and previously treated patients of lymph node and bone tuberculosis

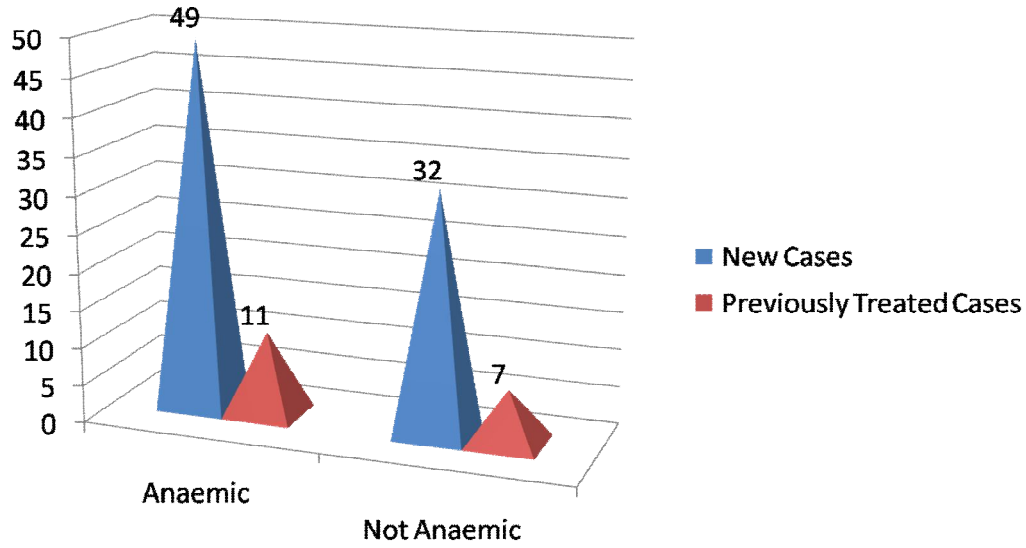

Figure 25: Occurence of anemia among new and previously treated patients of lymph node and bone tuberculosis

We observed that 60% of new patients and 61.1% of previously treated patients of lymph node and bone tuberculosis had haemoglobin concentration of less than 12 gram/dl.

Elevated ESR

ESR Status	New Cases	%	Previously Treated Cases	%
ESR > 40 mm/hr	69	85.18	16	88.88
ESR ≤ 40 mm/hr	12	27.16	2	11.11
Total	81	100	18	100
P value Fishers Exact Test			0.1513	

Table 10: ESR >40 mm Hg in new and previously treated patients

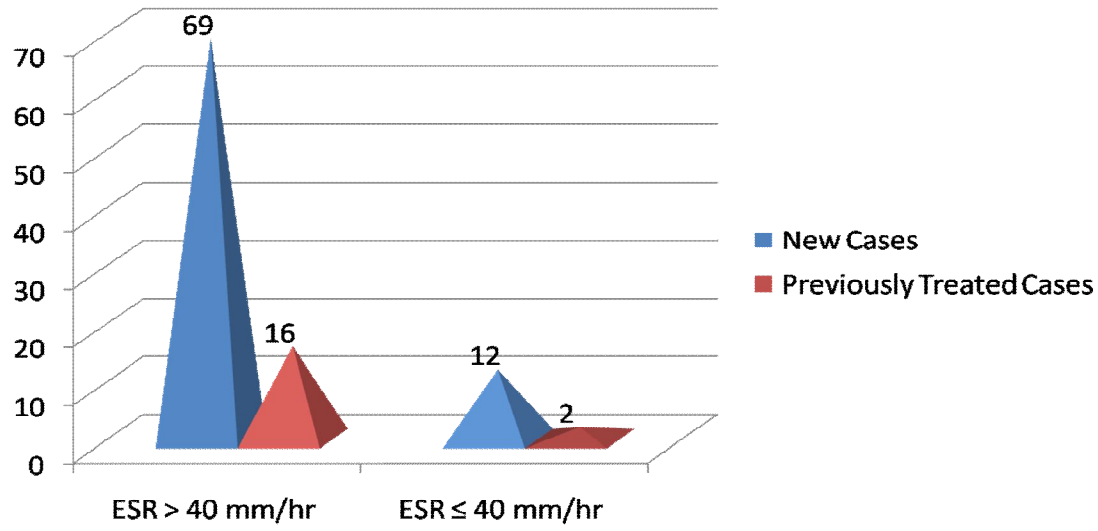

Figure 26: Elevated ESR in new and previously treated patients

In our study, we observed that 85%(n=85) of patients of lymph node and bone tuberculosis had ESR>40 mm Hg.

Smear for Acid Fast Bacillus

Smear Status	New Cases	%	Previously Treated Cases	%
Smear +ve	6	7.41	6	33.33
Smear -ve	75	92.59	12	66.67
Total	81	100	18	100
P value Chi Squared Test			0.0066	

Table 11: Direct Smear for AFB in new and previously treated patients

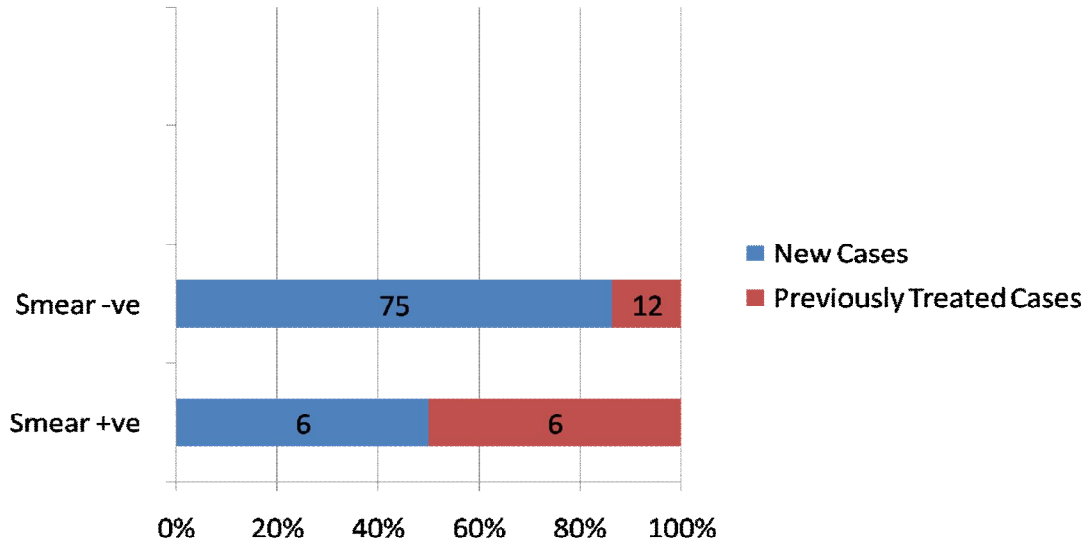

Figure 27: Direct Smear for AFB in new and previously treated patients

We observed that 7% of new patients(6 out of 81) and 33% of previously treated patients(6 out of 18) had positive smear for acid fast bacillus by modified Ziehl- Neelson staining and the difference is statistically significant.[p=0.0066]

LJ Culture

LJ Culture Status	New Cases	%	Previously Treated Cases	%
Culture positive	17	20.98	9	50
Culture negative	63	77.77	9	50
Total	81	100	18	100
P value Chi Squared Test			0.0055	

Table 12: LJ culture results in new and previously treated patients

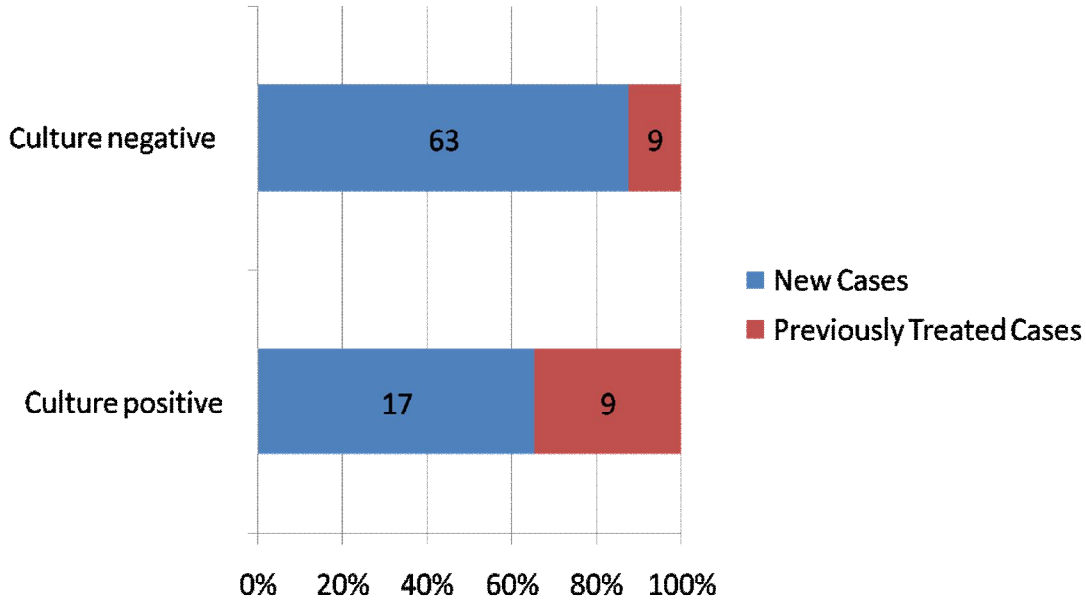

Figure 28: LJ culture results in new and previously treated patients

In our study 9 out of 18(50%) previously treated patients had positive culture in LJ medium and identified as mycobacterium tuberculosis. 17 out of 81(20.98%) of new patients had positive culture and the difference is statistically significant.[p=0.0055]

Drug Susceptibility Testing

DST Results	New Cases	%	Previously Treated Cases	%	P value Fishers Exact Test
Sensitive	14	82.35	4	44.44	0.0781
Resistant	3	17.64	5	55.55	
Total	17	100	9	100	

Table 13: Drug Susceptibility testing in new and previously treated patient

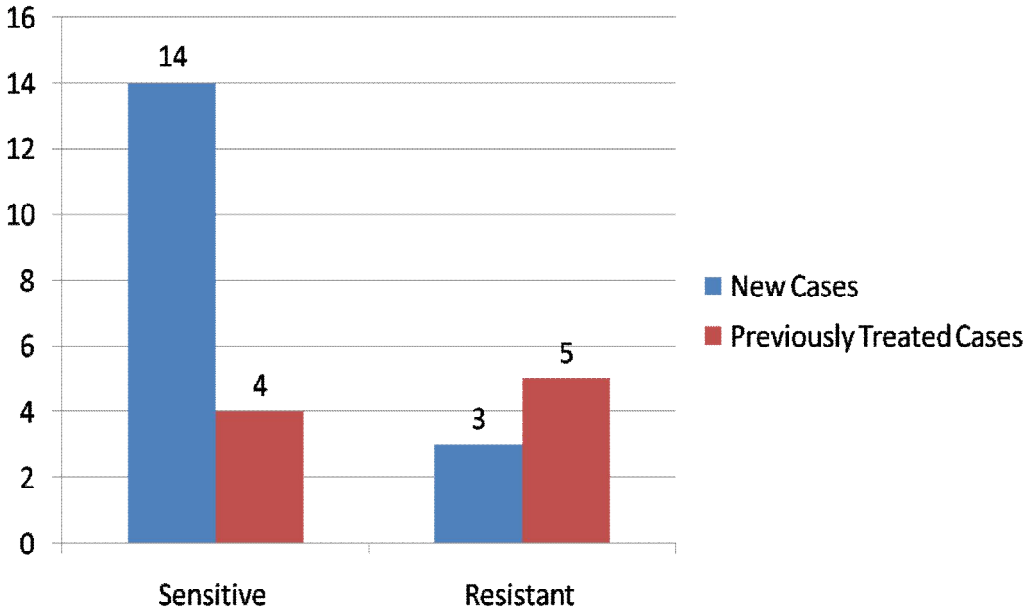

Figure 29: Drug Resistance in new and previously treated patients

In our study 14 patients out of 17 new patients had drug sensitive tuberculosis and 4 out of 9 previously treated patients. The drug resistance is 17.6% in new and 55.5 % in previously treated patients.

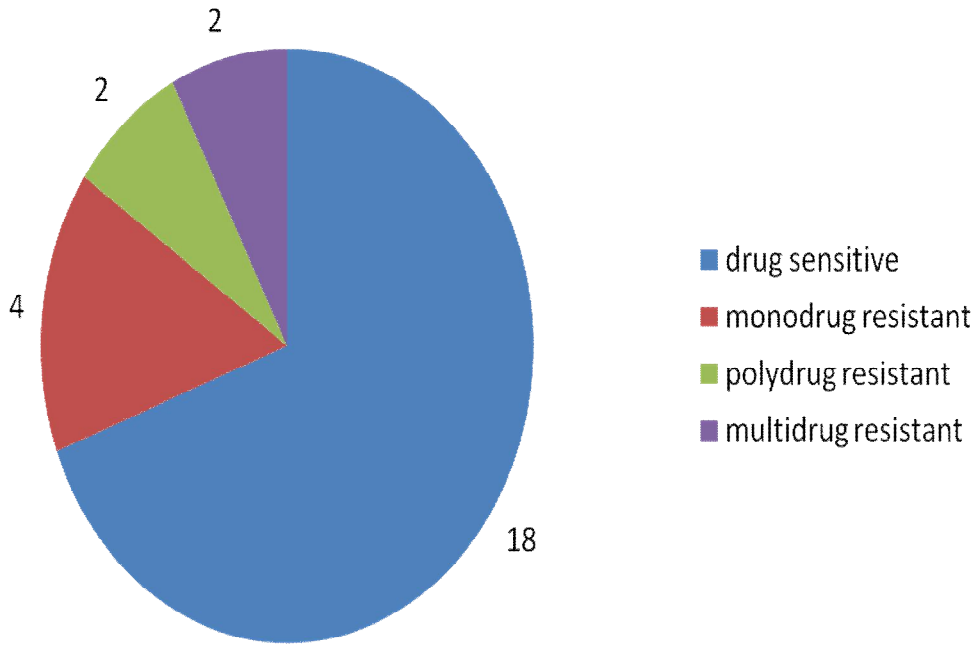

Figure 30: DST pattern (first line antituberculous drugs)

Out of 26 patients with culture positive results, 18 patients had drug sensitive tuberculosis. Among the 8 patients who had drug resistant tuberculosis, 2 had multidrug resistance (resistance to isoniazid and rifampicin) 2 had poly drug resistance (resistance to more than one antituberculous drug other than combination of isoniazid and rifampicin) and 4 had mono drug resistance (resistance to only one first line antituberculous drug).

Diabetes Mellitus

Diabetes Mellitus Status	New Cases	%	Previously Treated Cases	%
Diabetes Mellitus +	9	11.11	0	0.00
Diabetes Mellitus -	72	83.95	18	100.00
Total	81	100	18	100
P value Fishers Exact Test			0.1252	

Table 14: Diabetes mellitus in new cases and previously treated cases

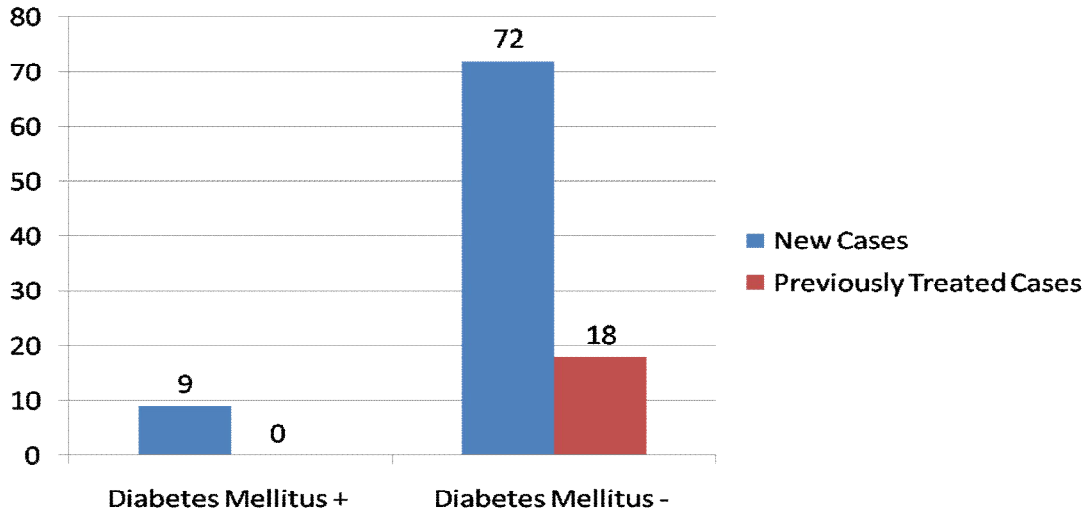

Figure 31: Diabetes mellitus in new cases and previously treated cases

In our study population 16% of the new cases had diabetes and none of the previously treated cases had diabetes.

Constitutional symptoms in diabetics and non diabetics

DM Vs Constitutional Symptoms	Constitutional Symptoms Present	Constitutional Symptoms Absent	Column Total
Diabetic	5	4	9
Non Diabetic	84	6	90
Row Total	89	10	99
P value Fishers Exact Test		0.0012	

Table 15: Constitutional symptoms in diabetics versus non diabetics

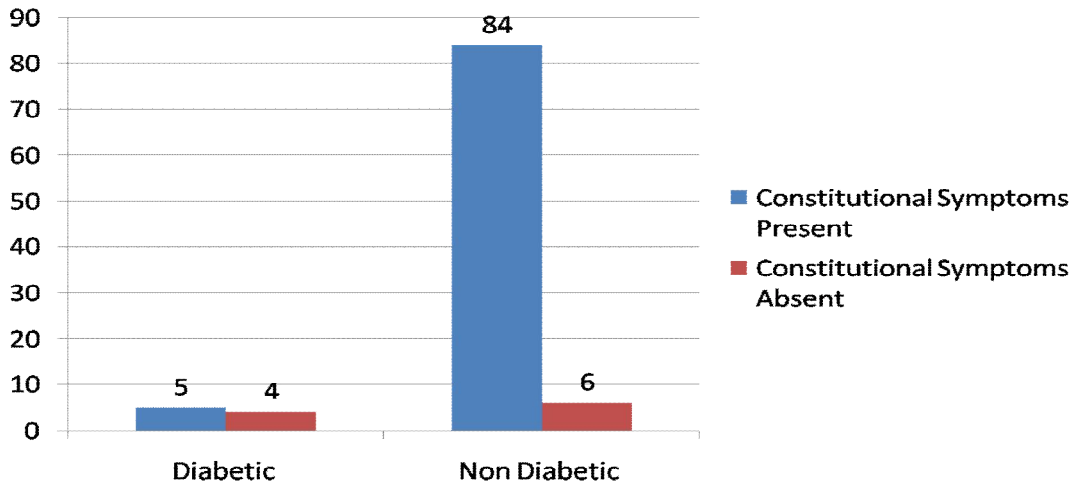

Figure 32: Constitutional symptoms in diabetics and non diabetics

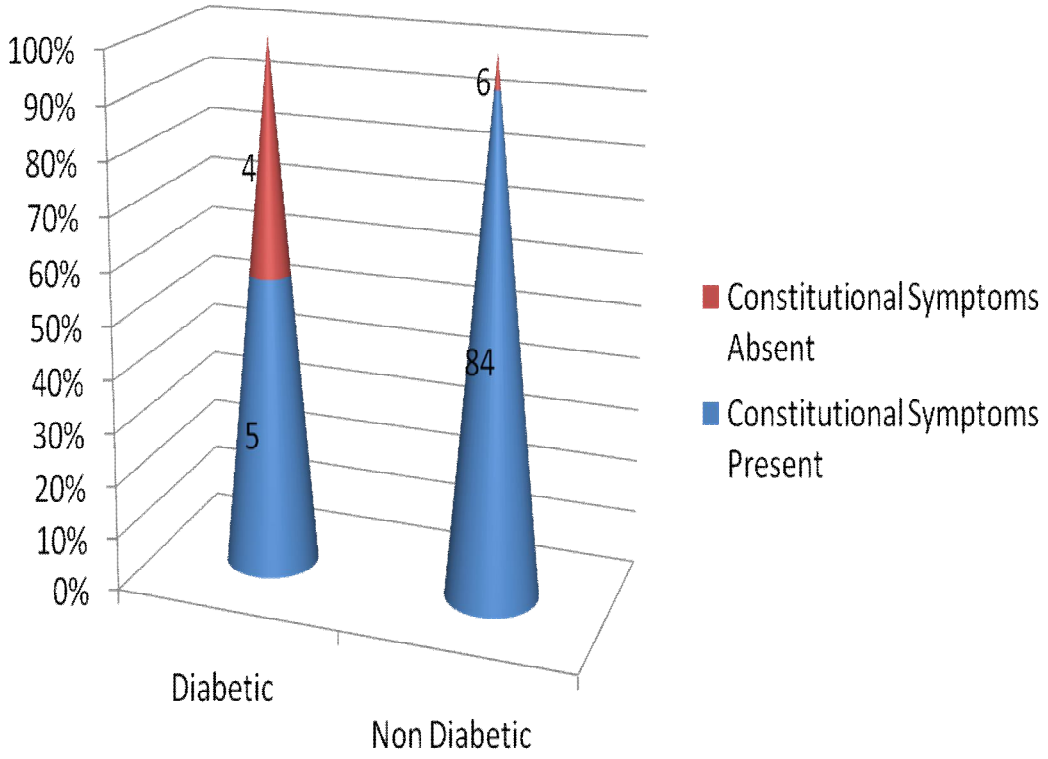

Figure 33: Percentage of diabetics and non diabetics with constitutional symptoms

We observed constitutional symptoms in 5 out of the 9 diabetic patients in our study. Among the non diabetics, out of 90 patients 84 had constitutional symptoms.

We observed constitutional symptoms to be present in 55.55% of diabetics and 93.33% of non diabetics. There is a difference in the occurrence of constitutional symptoms in patients of lymph node and bone tuberculosis if diabetes is a co morbid illness and the difference is statistically significant.[p=0.0012]

Smear for Acid fast bacilli and diabetes mellitus

DM Vs Smear Positivity	Smear positive	Smear Negative	Column Total
Diabetic	1	8	9
Non Diabetic	11	79	90
Row Total	12	87	99
P value Fishers Exact Test		> 0.9999	

Table 16: AFB smear positivity in diabetics and non diabetics

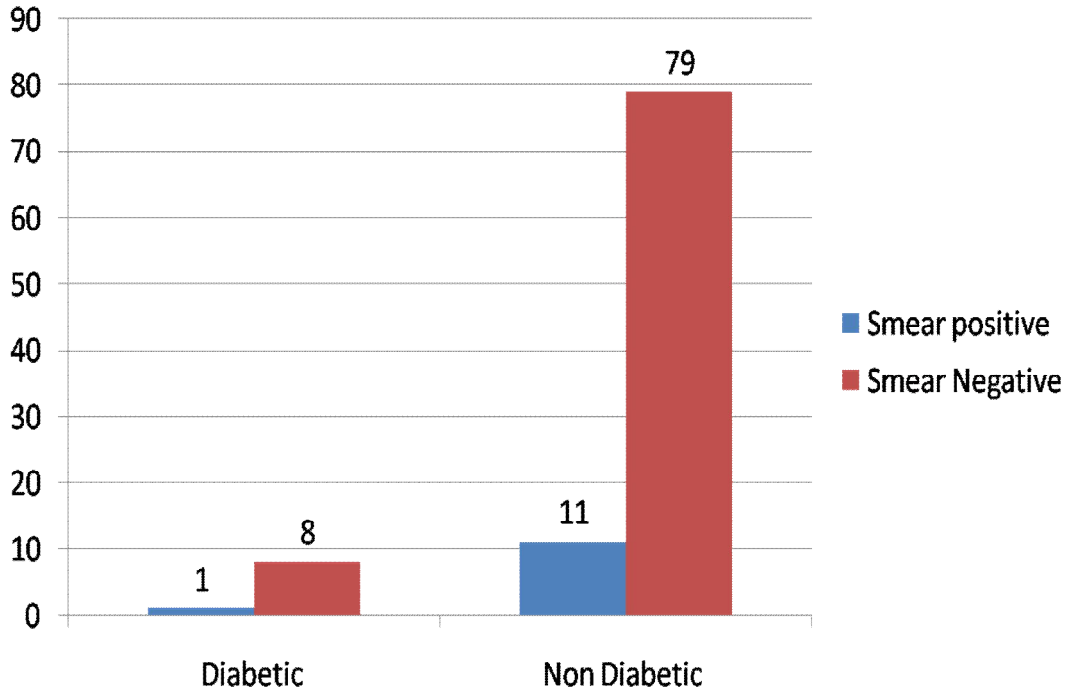

Figure 34: AFB smear positivity in diabetics and non diabetics

We observed that in 1 out of patients 9 diabetics direct smear for AFB was positive and in 11 out of 90 non diabetics direct smear for AFB was positive.

Comparison of culture growth and diabetes mellitus

DM Vs Culture Positivity	Culture Positive	Culture Negative	Column Total
Diabetic	3	6	9
Non Diabetic	23	67	90
Row Total	26	73	99
P value Fishers Exact Test		> 0.9999	

Table 17: Comparison of growth in culture and diabetes mellitus

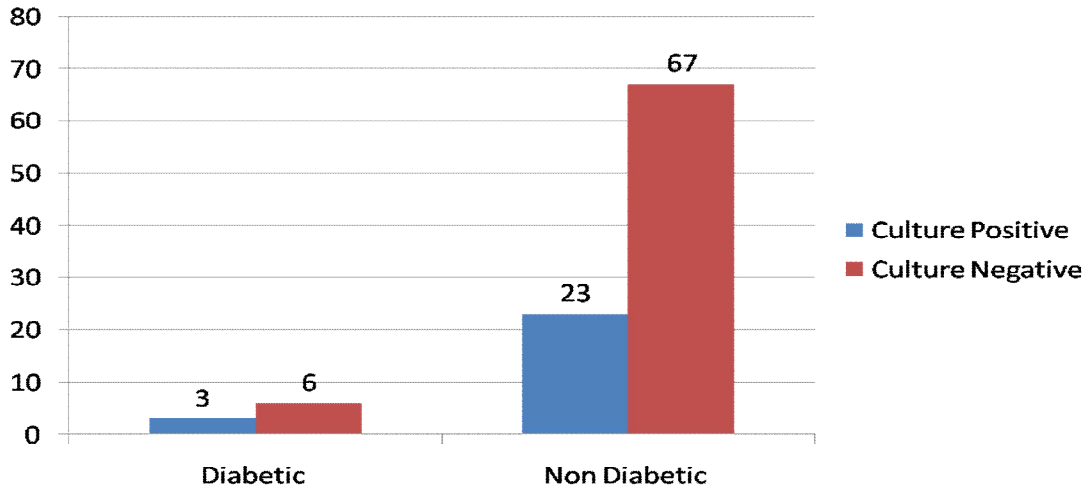

Figure 35: Co-relation between growth in culture and diabetes mellitus

We observed that 3 out of 9 diabetic patients (33.33%) had mycobacterium tuberculosis grown in culture and 23 out of 90 non diabetics(25.55%) had positive growth in LJ culure.

Drug resistance pattern in diabetics and non diabetics

DM Vs Drug Resistance	Drug Sensitive	Drug Resistant	Column Total
Diabetic	2	1	3
Non Diabetic	16	7	23
Row Total	18	8	26
P value Fishers Exact Test		> 0.9999	

Table 18: Drug resistance pattern in diabetics and non diabetics

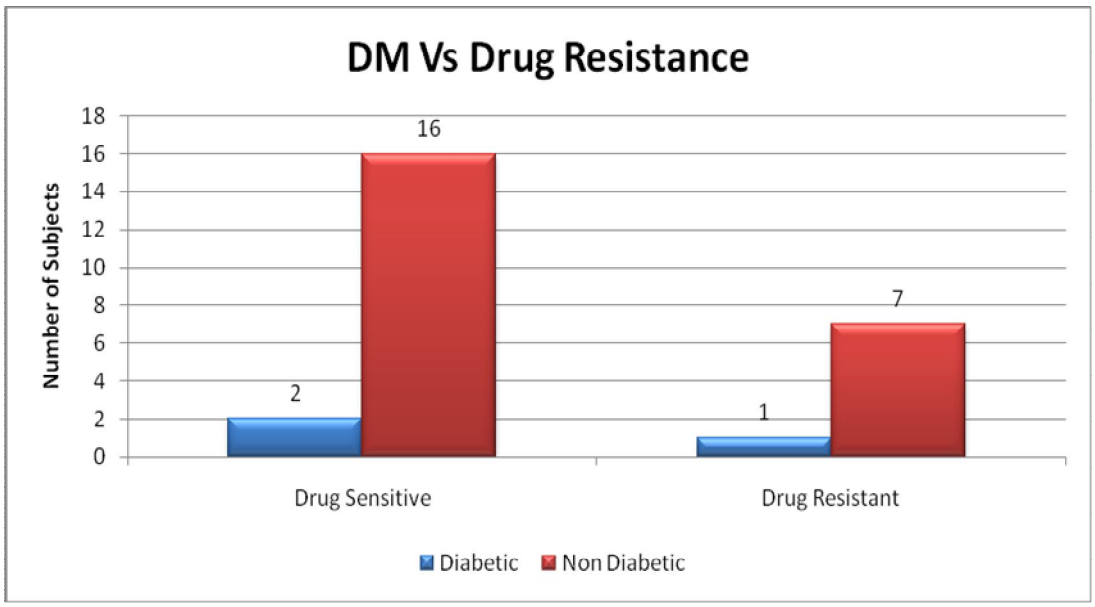

Figure 36: Drug resistant pattern in diabetics and non diabetics

We observed that out of 3 diabetic patients who had growth in culture 2 patients had drug sensitive tuberculosis and 1 patient had drug resistant tuberculosis.

HIV seropositivity in new and previously treated patients

HIV Status	New Cases	%	Previously Treated Cases	%
HIV +ve	7	8.64	3	16.66
HIV -ve	74	91.35	15	83.33
Total	81	100	18	100
P value Fishers Exact Test			0.3767	

Table 19: HIV seropositivity in new and previously treated patients

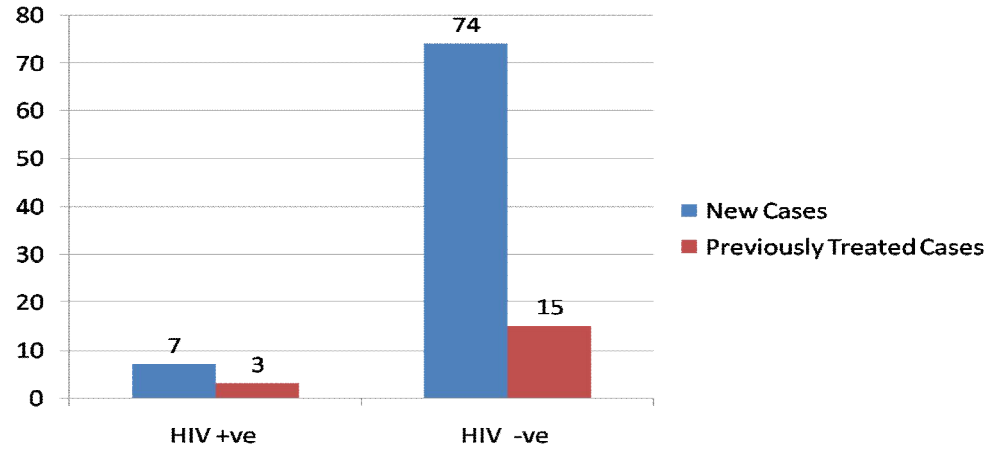

Figure 37: HIV seropositivity in new and previously treated patients

In our study, there were 7 HIV seropositive patients among new patients and 3 HIV seropositive patients among previously treated patients of lymph node and bone tuberculosis.

Constitutional symptoms in HIV patients

HIV Positivity Vs Constitutional Symptoms	Constitutional Symptoms Present	Constitutional Symptoms Absent	Column Total
HIV Positive	8	2	10
HIV Negative	81	8	89
Row Total	89	10	99
P value Fishers Exact Test		0.3188	

Table 20: Constitutional symptoms in HIV seropositive and seronegative patients

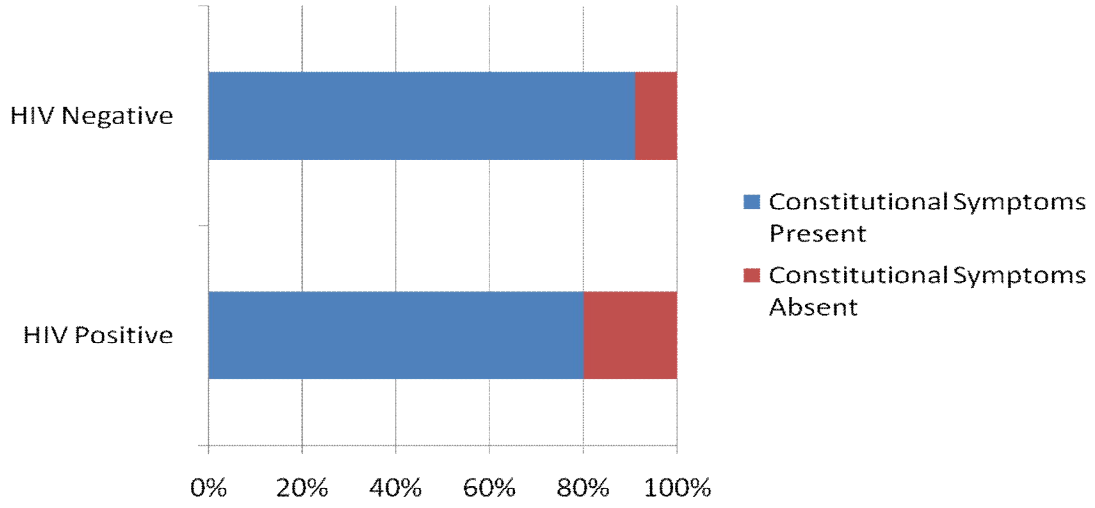

Figure 38 : Constitutional symptoms in HIV seropositive and seronegative patients

In our study 8 out of 10 HIV patients (80%) had constitutional symptoms and 81 out of 89 non HIV patients(91.01%) had constitutional symptoms.

Granulamotous histopathology in HIV and non HIV patients

HIV Positivity Vs HPE Positivity	HPE Granuloma	HPE non granuloma	Column Total
HIV Positive	4	6	10
HIV Negative	88	1	89
Row Total	92	7	99
P value Fishers Exact Test		0.0057	

Table 21: Granulomas in HIV and non HIV patients

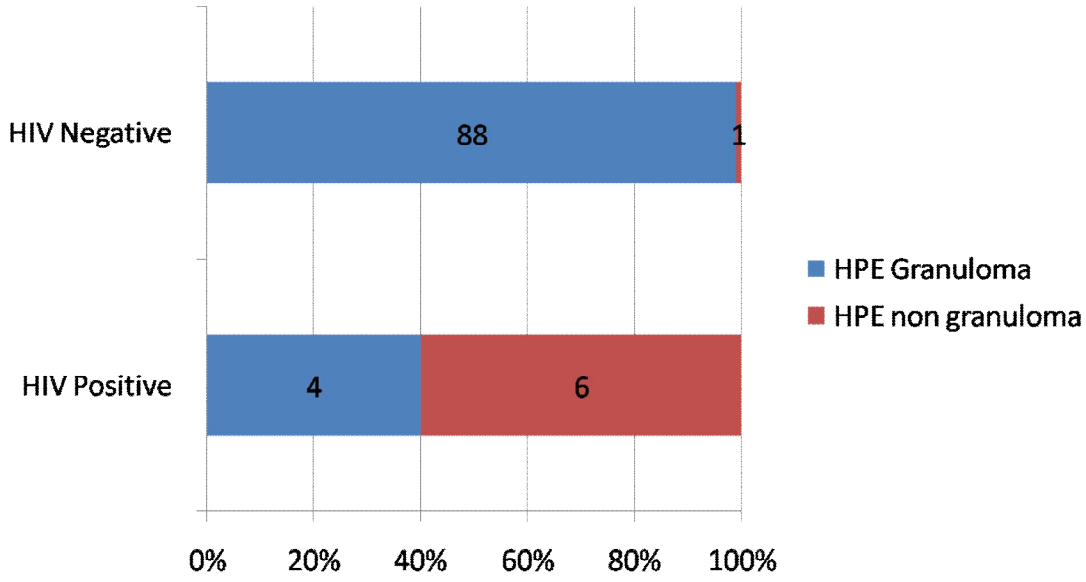

Figure 39: Granulomas in HIV and non HIV patients

In our study out of 10 HIV patients, 6(60%) did not show granulomas in histopathology. Among 89 patients who are seronegative for HIV 1(0.01%) did not show granuloma in histopathology.

Direct AFB smear in HIV and non HIV patients

HIV Positivity Vs Smear Positivity	Smear positive	Smear Negative	Column Total
HIV Positive	4	6	10
HIV Negative	6	83	89
Row Total	10	89	99
P value Fishers Exact Test		0.0108	

Table 22: Direct AFB smear in HIV and non HIV patients

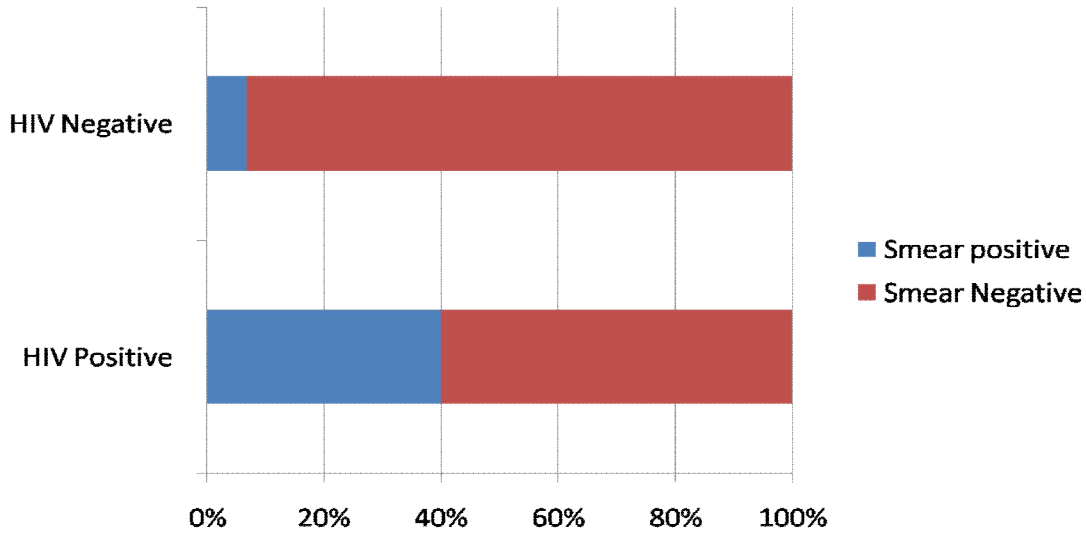

Figure 40: Direct AFB smear in HIV and non HIV patients

In our study 40 % of HIV patients and 6% of HIV non reactive patients had positive smear for AFB by modified Ziehl-Neelson staining.

LJ culture in HIV And non HIV patients

HIV Positivity Vs Culture Positivity	Culture Positive	Culture Negative	Column Total
HIV Positive	8	2	10
HIV Negative	18	71	89
Row Total	26	73	99
P value Fishers Exact Test		0.0005	

Table 23: LJ culture showing MTB growth in HIV and non HIV patients

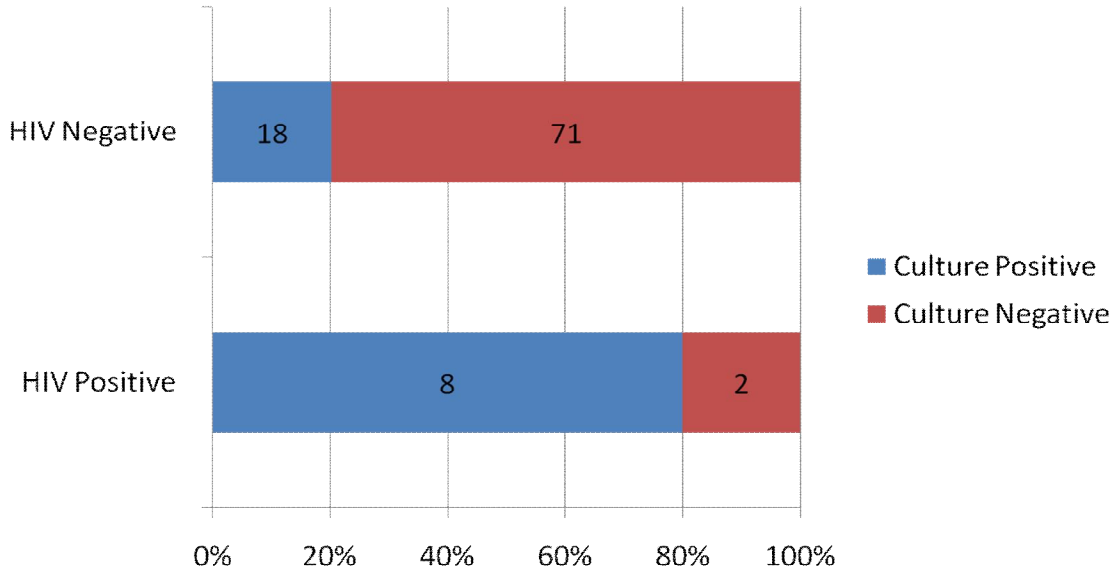

Figure 41: LJ culture showing MTB growth in HIV and non HIV patients

In our study out of 10 HIV patients, 8(80%) showed growth in culture and among 89 non HIV patients 18 patients (20%) showed growth in culture.

Drug resistance pattern in HIV patients

HIV Positivity Vs Drug Resistance	Drug Sensitive	Drug Resistant	Column Total
HIV Positive	6	3	9
HIV Negative	12	5	17
Row Total	18	8	26
P value Fishers Exact Test		> 0.9999	

Table 24: Drug resistance in HIV and non HIV patients

In our study out of 9 HIV patients who had MTB grown in LJ culture 3 patients had drug resistant tuberculosis. And among patients seronegative for tuberculosis among 17 culture positive patients, 5 patients had drug resistant tuberculosis.

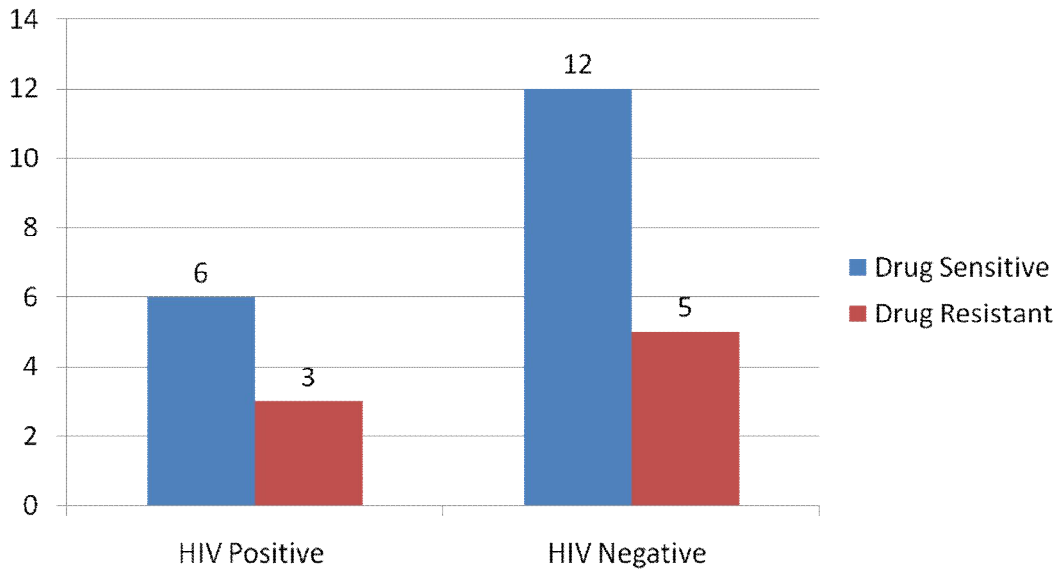

Figure 42: Drug resistant lymph node and bone TB in HIV and non HIV patients

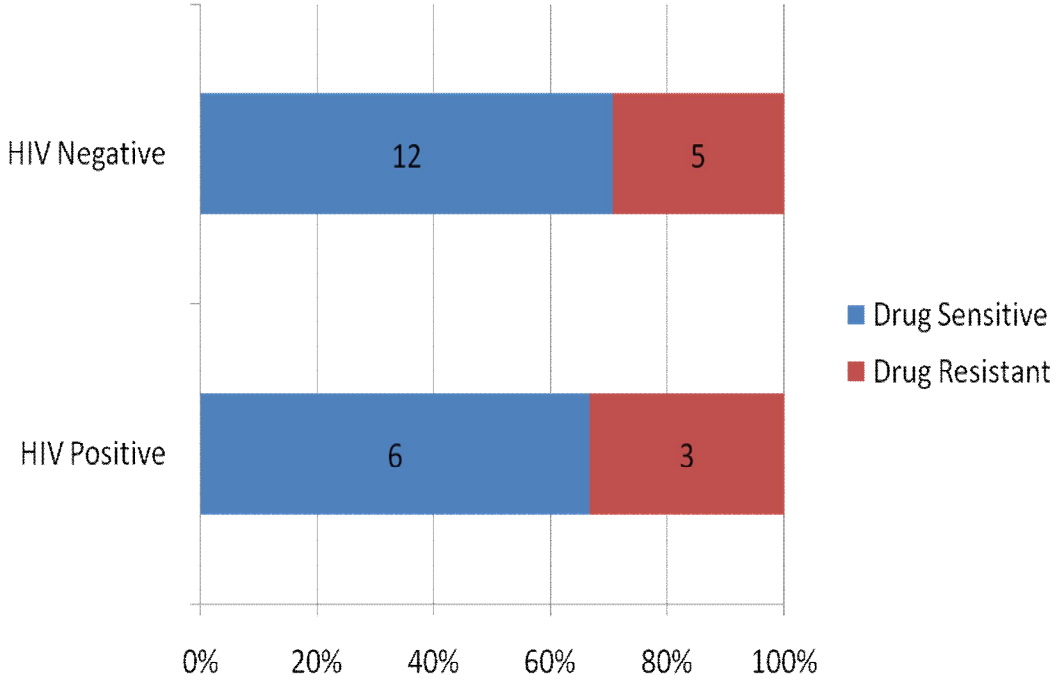

Figure 43:Percentage of drug resistant tuberculosis in HIV seropositive and seronegative patients

In our study, we observed that 3 patients out of 9 HIV patients who had mycobacterium tuberculosis grown in LJ culture had resistance atleast to one antituberculous drug. 33% of culture positive lymph node and bone tuberculosis in HIV patients were resistant to atleast one of first line antituberculous drugs.

Among HIV seronegative patients, among 17 patients who had growth in culture 5 cultures showed resistance to atleast one antituberculous drug. We observed that 29.4% of culture positive lymph node and bone tuberculosis in non HIV patients were resistant to atleast one of first line antituberculous drugs.

DISCUSSION

This study included 114 patients of clinical suspects of lymph node (n=83) and bone tuberculosis (n= 31).

Out of the 114 patients 92 patients had granulomas , 12 patients had non specific inflammation, 5 patients had carcinoma, 3 patients had lymphoma, 1 patient had acute inflammation and 1 patient had necrotic tissue on histopathological examination of the biopsy specimens.

It was observed LJ culture showed growth and isolates identified as Mycobacterium tuberculosis in 26 cases out of 114 cases. Out of 92 patients with granulomas on histopathology 19 were positive in LJ culture and out of 22 patients with non granulomas on histopathology 7 were positive in LJ culture. This observation is consistent with culture yields in earlier studies.

Definition for diagnosis of lymph node and bone tuberculosis:

A patient was defined as having lymph node / bone tuberculosis if either granulomas were present in histopatology or LJ culture showed growth and identified as mycobacterium tuberculosis or both.

19 cases were diagnosed as tuberculous based on both granulomas in histopathology and growth in LJ medium identified as Mycobacterium tuberculosis, 73 cases based on granulomas in histopathology alone and 7 cases based on LJ culture alone.

Out of 114 clinical suspects of lymph node and bone tuberculosis, 99 were diagnosed as tuberculous, lymph node(n=74) and bone(n=25).

Supportive evidence in lymph node and bone tuberculosis versus other diagnosis:

The contributions of contact history, constitutional symptoms, anemia and elevated ESR in the clinical suspicion of lymph node and bone tuberculosis were analysed.

It was observed that history of contact was present in 24 % of patients with tuberculosis and 20% of patients with other etiologies and constitutional symptoms were present in 81% of patients with tuberculosis and 80% of patients with other etiologies.

It was observed that anemia was present in 60 % of patients with tuberculosis and 60 % of patients with other etiologies and elevated ESR in 86 % of patients with tuberculosis and 87 % of patients with other diagnosis.

It was observed that the supportive evidences are almost equally distributed among cases of tuberculosis and other clinical suspects excluded from the case definition. Hence they play a marginal role in separating tuberculosis from other diagnosis.

Age distribution:

The peak age distribution observed in lymph node tuberculosis is 11 -20 years (47.29%), closely followed by 21-30 years (40.5%). These two age groups together constitute nearly 88% of cases of lymph node tuberculosis in our study.

The peak age distribution that we observed in bone tuberculosis is 31-40 years (40%), followed by 21-30 years (32%). These two age groups constitutes 72% of cases of bone tuberculosis.

Both lymph node and bone tuberculosis is relatively less common in age greater than 40 years. It was observed that only 10% of lymph node tuberculosis occurs in age greater than 40 years and 24% of bone tuberculosis occurs in age greater than 40 years.

The mean age of occurrence of lymph node tuberculosis and bone tuberculosis in our study is 25 years and 35 years respectively.

Gender distribution:

We observed a female preponderance in lymph node tuberculosis (63.51%) and male preponderance in bone tuberculosis (60%) which is statistically significant [p value -0.011].

In our study the ratio of male: female patients of 3 : 5.3 in lymph node tuberculosis and a male : female ratio of 3 : 2 in bone tuberculosis.

Sites of involvement in lymph node and bone tuberculosis:

In our study, it was observed that posterior cervical lymph node involvement was seen in 48%cases, anterior cervical in 42% cases, submandibular in 5% cases, axillary in 4% cases and inguinal in nearly 1%.

In bone tuberculosis, it was that observed 68% cases of bone tuberculosis in lower thoracic spine, 24% cases in lumbar spine and 8% cases in upper thoracic spine. The anatomic distribution of lymph node and bone tuberculosis are consistent with those observed in previous studies reviewed earlier.

Comparison of new patients and previously treated patients:

In this study it was observed that 27% new patients and 11.1% previously treated patients had history of contact with sputum positive case of pulmonary tuberculosis.

It was observed that constitutional symptoms were present in 71 out of 81 new patients (87.65%) of lymph node and bone tuberculosis and in all the previously treated patients.

It was observed that 60% of new patients and 61.1% of previously treated patients of lymph node and bone tuberculosis had haemoglobin concentration of less than 12 gram/dl.

In this study, it was observed that 85 % (n=85) of patients of lymph node and bone tuberculosis had ESR>40 mm Hg.

It was observed that 7% of new patients(6 out of 81) and 33% of previously treated patients (6 out of 18) had positive smear for acid fast bacillus by modified Ziehl- Neelson staining and the difference is statistically significant.[p=0.0066]

In this study 9 out of 18(50%) previously treated patients had positive culture in LJ medium and identified as mycobacterium tuberculosis. 17 out of 81(20.98%) of new patients had positive culture and the difference is statistically significant.[p=0.0055]

It is inferred from the above two observations that the bacillary load is higher in previously treated patients compared to new patients

In this study 14 patients out of 17 new patients had drug sensitive tuberculosis and 4 out of 9 previously treated patients had drug sensitive tuberculosis. The drug resistance is 17.6% in new and 55.5 % in previously treated patients.

Pattern of drug resistance:

Out of 26 patients with culture positive results, 18 patients had drug sensitive tuberculosis. Among the 8 patients who had drug resistant tuberculosis, two had multidrug resistance (resistance to isoniazid and rifampicin) two had poly drug resistance(resistance to more than one

antituberculous drug other than combination of isoniazid and rifampicin) and four had mono drug resistance(resistance to only one first line antituberculous drug).

Of the eight patients with drug resistance, six patients had lymph node tuberculosis and two patients had bone tuberculosis. Of the drug resistant lymph node tuberculosis, one patient had multidrug resistant tuberculosis, three patients had mono drug resistance and two patients had poly drug resistance.

Of the two patients with drug resistant bone tuberculosis, one had multidrug resistant tuberculosis and one had mono drug resistance.

Our results with reference to drug resistance in extra pulmonary tuberculosis were a little different from the study from North India by AK Maurya et al[36]., where they observed that 61.8% of new cases were susceptible to all drugs and 57.2% of previously treated cases were susceptible to all drugs. They observed that monoresistance and resistance to two drugs were more common in new cases whereas resistance to three drugs and resistance to four drugs were more common in previously treated cases. They observed that on the whole 39.9% of extrapulmonary tuberculosis cases were resistant to first line anti-tubercular drugs

Diabetes mellitus as a comorbidity in lymph node and bone tuberculosis:

In the study population 16% of the new cases had diabetes and none of previously treated cases had diabetes.

It was observed that constitutional symptoms were present in 5 out of the 9 diabetic patients in our study. Among the non diabetics, out of 90 patients 84 had constitutional symptoms.

Constitutional symptoms were present in 55.55% of diabetics and 93.33% of non diabetics. There is a difference in the occurrence of constitutional symptoms in patients of lymph node and bone tuberculosis if diabetes is a co morbid illness and the difference is statistically significant.[p=0.0012]

It was observed that in 1 out of 9 diabetics direct smear for AFB was positive and in 11 out of 90 non diabetics direct smear for AFB was positive.

It was observed that 3 out of 9 diabetic patients (33.33%) had mycobacterium tuberculosis grown in culture and 23 out of 90 non diabetics (25.55%) had positive growth in LJ culure.

It was observed that out of 3 diabetic patients who had growth in culture 2 patients had drug sensitive tuberculosis and 1 patient had drug resistant tuberculosis.

HIV in lymph node and bone tuberculosis:

In this study, there were 7 HIV seropositive patients among new patients and 3 HIV seropositive patients among previously treated patients of lymph node and bone tuberculosis. 8 out of 10 HIV patients(80%) had constitutional symptoms and 81 out of 89 non HIV patients(91.01%) had constitutional symptoms. Out of 10 HIV patients, 6(60%)did not show granulomas in histopathology. Among 89 patients who are seronegative for HIV 1(0.01%) did not show granuloma in histopathology.

In this study 40 % of HIV patients and 6% of HIV non reactive patients had positive smear for AFB by modified Ziehl-Neelson staining. Out of 10 HIV patients, 8(80%) showed growth in culture and among 89 non HIV patients 18 patients(20%) showed growth in culture.It is inferred that bacillary load is higher in HIV patients.

In this study, we observed that 3 patients out of 9 HIV patients who had mycobacterium tuberculosis grown in LJ culture had resistance atleast to one antituberculous drug. 33% of culture positive lymph node and bone tuberculosis in HIV patients were resistant to atleast one of first line antituberculous drugs.

Among HIV seronegative patients, 17 patients who had growth in culture 5 cultures showed resistance to atleast one antituberculous drug. We observed that 29.4% of culture positive lymph node and bone tuberculosis in non HIV patients were resistant to atleast one of first line antituberculous drugs.

CONCLUSION

1. **The case definition based on histology and microbiology was met by 86.8% of clinical suspects of lymph node and bone tuberculosis.**

2. **Most of the patients of lymph node tuberculosis were in the age group of 11-20 years and of bone tuberculosis were in the age group of 31-40 years.**

3. **Lymph node tuberculosis was more common in females with a male to female ratio of 3:5 and bone tuberculosis more common in males with a male to female ratio of 3:2.**

4. **There was histopathological evidence of granulomas in 80% of clinical suspects of lymph node and bone tuberculosis.**

5. **Mycobacterium tuberculosis was isolated from 22% of clinical suspects of lymph node and bone tuberculosis.**

6. **Of the culture isolates 23% showed non granulomas in histology, of these 60% were HIV seropositive and 40% diabetic. It is inferred that immune suppression interferes with eliciting a granulomatous response and hence in patients with immune suppression tuberculosis should be considered even in the absence of granulomas in histology.**

7. **The multi drug resistance rate was 22% in previously treated patients compared to none of the new patients.**

8. **The resistance rate in HIV patients was 37.5% and in HIV negative patients was 27.7%.**

9. **Lymph node and bone tuberculosis have a higher degree of drug resistance in previously treated patients and HIV seropositive patients. These groups can be considered as risk factors for drug resistance in lymph node and bone tuberculosis and can be targeted for drug susceptibility testing (DST).**

LIMITATIONS OF THE STUDY

1. The sample sizes of lymph node and bone tuberculosis are not equally distributed. Hence the results pertaining to culture yield and drug resistance cannot be interpreted giving equal weightage among the two groups.

2. Bone tuberculosis is represented only by tuberculosis of the spine.

3. There may be a selection bias because of the large proportion of referred cases reporting to our tertiary care hospital and the resistance rates cannot be extrapolated to the community at large.

4. The etiology of granulomas could be varied and is not specific to mycobacterium tuberculosis. Hence there is a possibility of overdiagnosis of mycobacterium tuberculosis.

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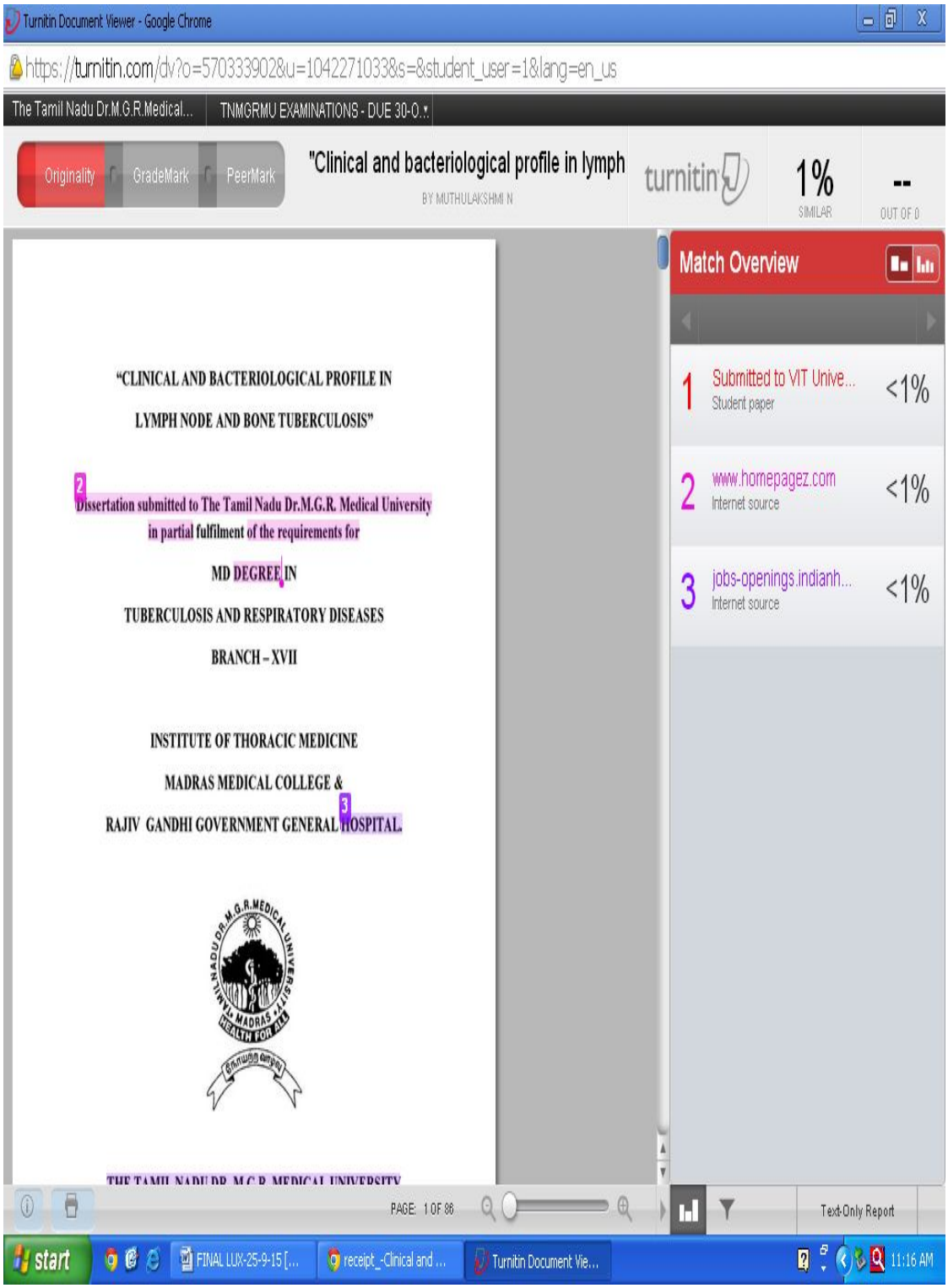
ABBREVIATIONS

MTB	–	Mycobacterium tuberculosis
MDR	–	Multi Drug Resistant
XDR	–	Extremely Drug Resistant
AFB	–	Acid Fast Bacillus
LJ medium	–	Lowenstein Jensen medium
SK medium	–	Selective Kirschner’s medium
HIV	–	Human Immunodeficiency Virus
NIRT	–	National Institute for Research in Tuberculosis
HPE	–	Histo Pathological Examination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Dissertation submitted to The Tamil Nadu Dr.M.G.R. Medical University
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BRANCH - XVII
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"CLINICAL AND BACTERIOLOGICAL PROFILE IN
LYMPH NODE AND BONE TUBERCULOSIS"

Dissertation submitted to The Tamil Nadu Dr.M.G.R. Medical University
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BRANCH – XVII

INSTITUTE OF THORACIC MEDICINE
MADRAS MEDICAL COLLEGE &
RAJIV GANDHI GOVERNMENT GENERAL HOSPITAL

THE TAMIL NADU DR. M.G.R. MEDICAL UNIVERSITY
CHENNAI, INDIA.
APRIL, 2016.

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI-3

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Fax : 044 25363970

CERTIFICATE OF APPROVAL

To
Dr. N. Muthulakshmi,
PG in Thoracic Medicine,
Institute of Thoracic Medicine,
Madras Medical College, Chennai-3.

Dear Dr. N. Muthulakshmi,

The Institutional Ethics Committee of Madras Medical College, reviewed and discussed your application for approval of the proposal entitled **"Clinical and Bacteriological profile in Lymph Node and Bone Tuberculosis"** No.31032014

The following members of Ethics Committee were present in the meeting held on 11.03.2014 conducted at Madras Medical College, Chennai-3.

1.	Dr. C. Rajendran, M.D.	-- Chairperson
2.	Prof. Kalaiselvi, MD Vice-Principal, MMC, Ch-3	-- Member Secretary
3.	Prof. Nandhini, M.D. Inst. of Pharmacology, MMC, Ch-3.	-- Member
4.	Prof. Bhavani Shankar, M.S. Prof & HOD of General Surgery, MMC, Ch-3.	-- Member
5.	Prof. V. Padmavathi, M.D. I/c Directory of Pathology, MMC, Ch-3.	-- Member
6.	Thiru. S. Govindasamy, BABL	-- Lawyer
7.	Tmt. Arnold Saulina, MA MSW	-- Social Scientist

We approve the proposal to be conducted in its presented form.

Sd/Chairman & Other Members

The Institutional Ethics Committee expects to be informed about the progress of the study, and SAE occurring in the course of the study, any changes in the protocol and patients information / informed consent and asks to be provided a copy of the final report.

Member Secretary, Ethics Committee

PATIENT INFORMATION SHEET

TITLE OF THE STUDY: "Clinical and bacteriological profile in lymph node and bone tuberculosis"

We are conducting a study on patients admitted in Rajiv Gandhi Government General Hospital, Chennai.

The purpose of this study is to study the clinical and and bacteriological characterisitics in patients with lymph node and bone tuberculosis.

We are selecting patients with lymph node/ bone tuberculosis in whom the treating doctor has suggested surgical intervention for diagnostic/therapeutic purposes. We collect sociodemographic details, clinical examination findings, relevant blood investigations and surgical specimens for histopathological and microbiological examination including culture for mycobacterium tuberculosis at national reference laboratory.

The privacy of the patients in the research will be maintained throughout the study. In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared.

Taking part in this study is voluntary. You are free to decide whether to participate in this study or to withdraw at any time; your decision will not result in any loss of benefits to which you are otherwise entitled.

The results of the special study may be intimated to you at the end of the study period or during the study if anything is found abnormal which may aid in the management or treatment.

Signature of Investigator Signature of Participant

Date :

PATIENT CONSENT FORM

Study Detail	:	"Clinical and bacteriological profile in lymph node and bone tuberculosis"
Study Centre	:	Rajiv Gandhi Government General Hospital, Chennai.
Patient's Name	:	
Patient's Age	:	
Identification Number	:	

Patient may check (√) these boxes

a) I confirm that I have understood the purpose of procedure for the above study. I have the opportunity to ask question and all my questions and doubts have been answered to my complete satisfaction. ☐

b) I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving reason, without my legal rights being affected. ☐

c) I understand that sponsor of the clinical study, others working on the sponsor's behalf, the ethical committee and the regulatory authorities will not need my permission to look at my health records, both in respect of current study and any further research that may be conducted in relation to it, even if I withdraw from the study I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from this study. ☐

d) I agree to take part in the above study and to comply with the instructions given during the study and faithfully cooperate with the study team and to immediately inform the study staff if I suffer from any deterioration in my health or well-being or any unexpected or unusual symptoms. ☐

e) I hereby consent to participate in this study. ☐

f) I hereby give permission to undergo detailed clinical examination, Radiographs, blood investigations and surgical procedure as required. ☐

Signature of Investigator — Signature of Participant

Date &time : — Name and address

Place:

ஆராய்ச்சி தகவல் தாள்

ஆராய்ச்சியின் பெயர் :

நிணநீர் முடிச்சு மற்றும் எலும்பு காச நோயின் நுண்ணுயிரியல் பற்றிய ஆராய்ச்சி

ஆராய்ச்சியாளர் பெயர் : மரு. ந. முத்துலட்சுமி

பங்கேற்பாளர் பெயர் :

சென்னை இராஜீவ் காந்தி அரசு பொது மருத்துவமனைக்கு வரும் நிணநீர் முடிச்சு மற்றும் எலும்பு காசே நோயின் நுண்ணுயிரியல் பற்றிய ஆராய்ச்சி.

முதல் நிலை மருந்துகளுக்கு கட்டுப்படாத காசநோய் உலக அளவில் அதிகரித்து வருகின்றது. நுரையீரல் அல்லாத பிற உறுப்புகளில் (நிண நீர் கட்டி மற்றும் எலும்பு) முதல் நிலை மருந்துகளுக்கு கட்டுப்படாத காசே நோய் பற்றி அறிவதே இந்த ஆராய்ச்சியின் நோக்கம்.

நீங்களும் இந்த ஆராய்ச்சியில் பங்கேற்க விரும்புகிறோம். இந்த ஆராய்ச்சியில் நிணநீர்க்கட்டி மற்றும் எலும்பு காச நோயின் முதல் நிலை மருந்து எதிர்ப்பு தன்மை பற்றி ஆராய்வோம் இதனால் தங்கள் நோயின் சிகிச்சைக்கு பாதிப்பு ஏற்படாது என்பதை தெரிவித்த கொள்கிறோம்.

முடிவுகளை அல்லது கருத்துகளை வெளியிடும் போதோ அல்லது ஆராய்ச்சியின் போதோ தங்களின் பெயரையோ அல்லது அடையாளங்களையோ வெளியிடமாட்டோம் என்பதையும் தெரிவித்து கொள்கிறோம்.

இந்த சிறப்பு பரிசோதனைகளின் முடிவுகளையும் நோயின் தன்மை பற்றியும் ஆராய்ச்சி முடியும்போது தங்களுக்கு அறிவிப்போம் என்பதையும் தெரிவித்துக் கொள்கிறோம்.

ஆராய்ச்சியாளர் கையொப்பம்

பங்கேற்பவர் கையொப்பம்

ஆராய்ச்சி தகவல் மற்றும் ஒப்புதல் படிவம்

ஆராய்ச்சி தலைப்பு

எலும்பு மற்றும் நிணநீர்முடிச்சின் காசநோய் மருத்துவ மற்றும் நுண்ணுயிரியல் சுயவிவரத்தை அறிதல்

ஆராய்ச்சியாளர் பெயர் : மரு. முத்துலட்சுமி, MD (TB & RD)

இந்த ஆராய்ச்சியின் விவரங்களும் அதன் நோக்கமும் முழுமையாக எனக்கு தெளிவாக விளக்கப்பட்டது. எனக்கு விளக்கப்பட்ட விஷயங்களை புரிந்துகொண்டு நான் எனது சம்மதத்தை தெரிவிக்கிறேன்.

இந்த ஆராய்ச்சியின் நோக்கம் நிணநீர் முடிச்சின் மற்றும் எலும்பு காச நோய் ஸ்மியர் மற்றும் வளர்ப்பு தேர்மறைத் தன்மை நிகழ்வு கண்டுபிடித்தல் மற்றும் மருந்து எதிர்ப்பு தன்மை கண்டுபிடித்தல்.

இந்த ஆராய்ச்சியில் பிறரின் நிர்பந்தமின்றி என் சொந்த விருப்பத்தின்பேரில் நான் பங்கு பெறுகின்றேன். இந்த ஆராய்ச்சியில இருந்து நான் எந்நேரமும் பின் வாங்கலாம் என்பதையும் அதனால் எந்த பாதிப்பும் ஏற்படாது என்பதையும் நான் புரிந்துகொண்டேன்.

நான் என்னுடைய சுய நினைவுடனும் மற்றும் முழு சுதந்திரத்துடனும் இந்த மருத்துவ ஆராய்ச்சியில் என்னை சேர்த்துக்கொள்ள சம்மதிக்கிறேன்.

முடிவுகளை அல்லது கருத்துகளை வெளியிடும்போதோ அல்லது ஆராய்ச்சியின் போதோ தங்களது பெயரையோ அல்லது அடையாளங்களையோ வெளியிடமாட்டோம் என்பதையும் தெரிவித்துக் கொள்கிறோம்.

ஆராய்ச்சியாளர் கையொப்பம் பங்கெடுப்பாளர் கையொப்பம்

நாள் :

இடம் :

PROFORMA

Name

Age

Sex

IP/OP Number

Address

Clinical History

Presenting complaints

Duration of symptoms

History of constitutional symptoms

History of contact with sputum positive case of tuberculosis

Previous history of treatment for tuberculosis/ history of diabetes mellitus and other comorbid illness.

Clinical Examination:

Investigations:

For all patients

- Chest X ray PA view
- Hemogram
- Random Blood Sugar
- HIV antibody testing

If indicated

- Fasting Blood Sugar
- Postprandial Blood Sugar
- Renal Function Test
- Liver Function Test
- Sputum for Acid Fast Bacilli
- Ultrasonogram Abdomen/Neck
- X ray Lumbo sacral/dorsal spine
- MRI Spine

Histopathological Examination:

Microbiological Examination:

Direct Smear for AFB:

LJ Culture:

Drug Sensitivity Pattern:

s.no	age	sex	lymph no	Prior ATT	DM	HIV	H/O conta	Constitut	anemia	esr>40	HPE	Smear sta	culture st	DST patte
1	22	Female	lymph node	no	no	no	yes	yes	yes	yes	granuloma	negative	positive	sensitive
2	16	Female	lymph node	no	no	no	no	yes	yes	yes	granuloma	negative	positive	sensitive
3	21	Female	lymph node	no	no	no	no	yes	yes	yes	granuloma	negative	negative	-
4	16	male	lymph node	yes	no	no	no	yes	yes	yes	granuloma	negative	positive	sensitive
5	55	male	lymph node	no	no	yes	no	yes	yes	yes	non specific	positive	positive	resistant
6	15	Female	lymph node	no	no	no	yes	yes	yes	no	nonspecific	negative	positive	sensitive
7	14	female	lymph node	yes	no	no	no	yes	no	yes	granuloma	negative	negative	-
8	25	female	lymph node	no	no	no	no	yes	no	yes	granuloma	negative	negative	-
9	12	male	lymph node	no	no	no	yes	yes	no	no	granuloma	negative	negative	-
10	43	male	lymph node	no	yes	no	yes	yes	yes	yes	lymphoma	negative	negative	-
11	35	female	lymph node	yes	no	no	no	yes	yes	yes	granuloma	negative	negative	-
12	24	Female	lymph node	no	no	no	no	yes	no	yes	granuloma	negative	negative	-
13	19	male	lymph node	no	no	yes	no	yes	yes	yes	nonspecific	positive	positive	sensitive
14	22	female	lymph node	no	no	no	no	yes	yes	yes	granuloma	negative	negative	-
15	18	female	lymph node	no	no	no	no	yes	no	yes	granuoma	negative	negative	-
16	11	male	lymph node	no	no	no	no	yes	no	yes	nonspecific	negative	negative	-
17	16	Female	lymph node	no	no	no	yes	yes	yes	yes	granuloma	negative	negative	-
18	54	male	lymph node	yes	no	yes	no	yes	yes	yes	nonspecific	positive	positive	resistant
19	15	male	lymph node	no	no	no	no	yes	no	yes	granuloma	negative	negative	-
20	9	male	lymph node	no	no	no	no	yes	yes	yes	nonspecific	negative	negative	-
21	65	male	lymph node	no	yes	no	no	yes	no	no	carcinoma	negative	negative	-
22	55	male	lymph node	no	no	no	no	no	yes	yes	granuloma	negative	positive	sensitive
23	28	male	lymph node	no	no	no	no	yes	no	yes	granuloma	negative	negative	-
24	14	Female	lymph node	no	no	no	yes	no	no	no	granuloma	negative	negative	-
25	16	Female	lymph node	no	no	yes	yes	no	yes	no	nonspecific	positive	positive	sensitive
26	55	Female	lymph node	no	yes	no	no	no	yes	yes	carcinoma	negative	negative	-
27	22	Female	lymph node	no	no	no	no	yes	no	yes	granuloma	negative	negative	-
28	62	male	lymph node	no	yes	no	no	no	no	yes	carcinoma	negative	negative	-

29	28	male	lymph node	no	no	no	no	no	no	yes	granuloma	positive	positive	sensitive
30	13	male	lymph node	yes	no	no	yes	yes	no	no	granuloma	positive	positive	resistant
31	23	female	lymph node	no	no	no	no	yes	yes	yes	granuloma	negative	negative	-
32	29	male	lymph node	no	no	no	no	yes	no	no	granuloma	negative	negative	-
33	12	Female	lymph node	yes	no	no	yes	yes	yes	yes	granuloma	negative	positive	resistant
34	26	Female	lymph node	no	no	no	no	yes	no	yes	granuloma	negative	negative	-
35	46	male	lymph node	no	yes	no	no	no	no	no	granuloma	negative	negative	-
36	13	Female	lymph node	no	no	yes	yes	yes	no	no	granuloma	negative	positive	resistant
37	15	Female	lymph node	no	no	no	no	yes	no	no	granuloma	negative	negative	-
38	14	male	lymph node	no	no	no	no	yes	yes	yes	granuloma	negative	negative	-
39	28	Female	lymph node	no	no	no	no	yes	yes	yes	granuloma	negative	negative	-
40	26	Female	lymph node	yes	no	no	no	yes	yes	yes	granuloma	negative	negative	-
41	24	male	lymph node	no	no	no	no	yes	no	yes	granuloma	negative	negative	-
42	25	female	lymph node	no	no	no	yes	yes	no	yes	granuloma	positive	positive	sensitive
43	57	female	lymph node	no	yes	no	no	no	yes	yes	granuloma	negative	negative	-
44	15	Female	lymph node	no	no	no	no	yes	yes	yes	granuloma	negative	negative	-
45	13	male	lymph node	no	no	no	no	yes	no	no	granuloma	negative	negative	-
46	15	female	lymph node	no	no	no	no	yes	yes	yes	lymphoma	negative	negative	-
47	18	female	lymph node	no	no	no	no	yes	yes	yes	granuloma	negative	negative	-
48	22	male	lymph node	no	no	no	no	yes	no	yes	granuloma	negative	negative	-
49	14	male	lymph node	no	no	no	no	yes	yes	yes	granuloma	negative	negative	-
50	19	female	lymph node	yes	no	no	no	yes	yes	yes	granuloma	positive	negative	-
51	22	Female	lymph node	no	no	no	no	yes	yes	yes	granuloma	negative	negative	-
52	20	Female	lymph node	no	no	no	yes	yes	no	yes	granuloma	negative	negative	-
53	21	Female	lymph node	no	no	no	no	yes	no	no	granuloma	negative	negative	-
54	24	female	lymph node	no	no	no	no	no	yes	yes	granuloma	negative	negative	-
55	27	male	lymph node	no	no	no	no	yes	no	yes	granuloma	negative	negative	-
56	56	male	lymph node	no	yes	no	no	yes	yes	yes	granuloma	negative	negative	-
57	22	Female	lymph node	no	no	no	yes	yes	yes	yes	granuloma	negative	negative	-

58	20	Female	lymph node	no	no	no	no	yes	yes	yes	granuloma	negative	negative	-
59	23	male	lymph node	no	no	yes	no	yes	yes	yes	nonspecific	negative	positive	sensitive
60	16	Female	lymph node	no	no	no	no	yes	yes	yes	granuloma	negative	negative	-
61	24	male	lymph node	no	no	no	no	yes	yes	yes	granuloma	negative	negative	-
62	13	male	lymph node	no	no	yes	no	yes	yes	yes	granuloma	negative	negative	-
63	20	female	lymph node	no	no	no	no	yes	no	no	granuloma	negative	negative	-
64	15	male	lymph node	no	no	no	yes	yes	yes	yes	granuloma	negative	negative	-
65	23	female	lymph node	yes	no	no	no	yes	yes	yes	granuloma	negative	positive	sensitive
66	27	Female	lymph node	no	no	no	no	yes	no	no	granuloma	negative	negative	-
67	17	female	lymph node	no	no	no	no	yes	yes	no	granulma	negative	negative	-
68	25	Female	lymph node	no	no	no	yes	yes	yes	yes	granuloma	negative	negative	-
69	53	male	lymph node	no	yes	no	no	no	yes	yes	granuloma	negative	negative	-
70	21	female	lymph node	no	no	no	no	yes	yes	yes	granuloma	negative	negative	-
71	14	male	lymph node	no	no	no	no	yes	yes	no	granuloma	negative	negative	-
72	16	female	lymph node	yes	no	no	no	yes	yes	yes	granuloma	negative	negative	-
73	29	female	lymph node	no	no	yes	no	no	yes	yes	granuloma	negative	positive	sensitive
74	27	male	lymph node	no	no	no	no	yes	no	no	granuloma	negative	negative	-
75	14	Female	lymph node	no	no	no	no	yes	no	no	granuloma	negative	negative	-
76	22	female	lymph node	no	no	no	yes	yes	yes	yes	granuloma	negative	negative	-
77	19	female	lymph node	no	no	no	no	yes	yes	no	granuloma	negative	negative	-
78	15	Female	lymph node	no	no	no	no	yes	no	no	acute inflam	negative	negative	-
79	18	female	lymph node	no	no	no	no	yes	yes	yes	granuloma	negative	negative	-
80	65	male	lymph node	no	yes	no	no	yes	yes	yes	carcinoma	negative	negative	-
81	19	Female	lymph node	no	no	no	no	yes	yes	yes	granuloma	negative	positive	sensitive
82	44	female	lymph node	no	yes	no	yes	yes	yes	yes	granuloma	negative	positive	resistant
83	15	male	lymph node	no	no	no	no	yes	yes	yes	granuloma	negative	negative	-
84	27	male	spine	yes	no	no	no	yes	no	no	granuloma	negative	negative	-
85	35	male	spine	no	no	no	no	yes	yes	yes	nonspecific i	negative	negative	-
86	42	female	spine	yes	no	yes	no	yes	yes	yes	nonspecific i	negative	positive	sensitive

87	27	male	spine	yes	no	no	no	yes	no	yes	granuloma	positive	positive	resistant
88	33	female	spine	no	no	no	yes	yes	yes	no	granuloma	negative	negative	-
89	42	male	spine	no	no	no	no	yes	yes	yes	granuloma	negative	negative	-
90	9	male	spine	no	no	no	no	yes	yes	yes	lymphoma	negative	negative	-
91	17	male	spine	no	no	no	yes	yes	no	yes	nonspecific i	negative	negative	-
92	48	female	spine	no	yes	no	yes	yes	yes	yes	granuloma	negative	negative	-
93	38	male	spine	no	no	no	yes	yes	yes	yes	granuloma	negative	positive	sensitive
94	26	male	spine	yes	no	no	no	yes	no	yes	granuloma	negative	negative	-
95	36	male	spine	no	no	no	no	yes	no	yes	granuloma	negative	negative	-
96	38	male	spine	yes	no	no	no	yes	no	yes	granuloma	positive	positive	sensitive
97	42	Female	spine	yes	no	yes	no	yes	yes	yes	granuloma	negative	negative	-
98	61	male	spine	yes	no	no	no	no	yes	yes	carcinoma	negative	negative	-
99	27	male	spine	no	no	no	yes	yes	no	no	granuloma	negative	negative	-
100	24	female	spine	yes	no	no	no	yes	yes	yes	granuloma	positive	positive	resistant
101	35	male	spine	no	no	no	yes	yes	no	no	granuloma	negative	negative	-
102	52	male	spine	no	yes	no	yes	yes	yes	yes	granuloma	negative	positive	senstive
103	39	female	spine	no	no	no	yes	yes	no	no	granuloma	negative	negataive	-
104	23	female	spine	no	yes	no	no	no	yes	yes	granuloma	positive	positive	sensitive
105	32	male	spine	yes	no	no	no	yes	no	yes	granuloma	negative	negative	-
106	41	male	spine	no	no	no	yes	yes	no	yes	necrotic tiss	negative	negative	-
107	34	female	spine	yes	no	no	no	yes	yes	yes	granuloma	negative	negative	-
108	29	male	spine	no	no	no	no	yes	yes	yes	nonspecific i	negative	negative	-
109	32	male	spine	no	no	no	no	yes	no	no	granuloma	negative	negative	-
110	26	female	spine	no	no	no	no	yes	yes	yes	granuloma	negative	negative	-
111	64	male	spine	no	yes	no	no	yes	no	no	granuloma	negative	negative	-
112	36	male	spine	no	no	no	yes	yes	yes	yes	granuloma	negative	negative	-
113	54	female	spine	no	no	no	no	yes	yes	yes	granuloma	negative	negative	-
114	24	male	spine	no	no	no	no	yes	no	yes	granuloma	negative	negative	-